

DRUGS AND MEDICINAL PREPARATIONS

A MANUAL FOR PHYSICIANS

Fourth Edition
Revised and Enlarged

V/O "MEDEXPORT"

Chapter I

MEDICINAL AGENTS ACTING PREEMINENTLY ON THE CENTRAL NERVOUS SYSTEM

I ANESTHETICS AND HYPNOTICS

A Agents for inhalation anesthesia

ETHER (Aether)

Ethyl ether (Aether aethylicus) or sulphuric ether (Aether sulfuricus) die thyl ether $C_2H_5 = O = C_2H_5$

Two preparations are available medicinal ether (Aether medicinalis) and anesthetic ether (Aether pro narcosi Aether anaestheticus) The first is intended for external and oral use laboratory work the preparation of tinctures and extracts etc Ether for anesthesia is subjected to special purification during the production process its specific gravity (0.714—0.715) is somewhat less than that of medicinal ether (0.714—0.718) and it boils over a shorter range (34—35° as compared with 34—36°)

Both preparations are colourless transparent very mobile highly flammable liquids of characteristic odour and burning taste Soluble in 12 parts of water miscible in all proportions with alcohol benzene petroleum ether and fatty and volatile oils

Ether vapour is highly flammable and forms explosive mixtures with oxygen air and nitrous oxide

Aether pro narcosi is used in surgical practice for inhalation anesthesia it is sometimes used in an oil enema (chiefly in relieving pain in childbirth)

Up to 1 ml of ether is sometimes administered subcutaneously as a stimulant in cases of depression of cardiac action and respiration, the action is reflex in character Ether or "ether drops" are sometimes prescribed orally for the same purpose as well as to arrest vomiting

Ether is an ingredient along with chloroform of an inhalation mixture ("anti smoke mixture") used in cases of poisoning with irritating arsines

For inhalation anesthesia ether is used alone or in combination with nitrous oxide and oxygen

Ether anesthesia is relatively safe and is easily controlled When the correct dosage is used it does not cause essential changes in circulation or respiration The skeletal muscles are relaxed well

Ether vapour however irritates the mucous membrane of the respiratory passages and causes a considerable intensification of secretion by the salivary and bronchial glands Irritation of the respiratory passages may be accompanied

at the beginning of anesthesia by reflex changes in respiration and by laryngo spasm. In order to avoid these complications anesthetization is often begun with nitrous oxide and oxygen with the subsequent use of ether. Secretion is limited by the preliminary administration of atropine.

Curare drugs ("relaxants") can be used in order to secure better relaxation of the skeletal muscles. It must be borne in mind that their action is usually accentuated by ether and accordingly the dosage must be lowered (see p. 122).

Ether anesthesia ordinarily causes no complications. However because of its irritating action on the mucous membranes of the respiratory passages subsequent bronchopneumonia is possible.

Contraindications to the use of ether anesthesia: pulmonary tuberculosis, acute diseases of the respiratory passages, elevated intracranial pressure, cardiovascular diseases with substantial elevation of the blood pressure and decompensated cardiac action, severe kidney disease, general malnutrition, diabetes and acidosis.

To be stored in tightly stoppered bottles of amber glass in a cool place away from fire, observing safety precautions (List B). Fit for use for 6 months.

Anesthetic ether is supplied in hermetically sealed bottles of amber glass of 100 ml capacity filled to the top and with metal foil under the stopper.

For anesthesia only ether from bottles opened immediately before the operation can be used. Under the influence of light, air and moisture harmful products are formed (peroxides, aldehydes and ketones) which intensely irritate the respiratory passages.

Maximal doses of ether for oral administration (for adults): single — 0.33 ml (20 drops) daily — 1 ml (60 drops).

CHLOROFORM (Chloroformium)

Trichloromethane CHCl_3

Synonym: Formyl trichloride.

Colourless transparent heavy mobile, volatile liquid with characteristic odour and sweet burning taste. Miscible in all proportions with absolute alcohol, ether, benzene and many volatile oils, difficultly soluble in water (1:200). Specific gravity 1.477—1.486. Boiling point 59.5—62°.

Chloroform vapour is nonflammable and does not explode. Chloroform is decomposed by the action of light, air, moisture and heat, forming phosgene, chlorine, formic and hydrochloric acids.

Two preparations are available: 1) chloroform (Chloroformium) and 2) anesthetic chloroform (Chloroformium pro narcosi, Chloroformium anaestheticum). The first is used only for external application and laboratory work. The second is specially purified and is intended for inhalation anesthesia. 0.6—1% absolute alcohol is added as a stabilizer.

Chloroform is a very potent anesthetic but has a relatively high toxicity. It may cause an impairment of the cardiac rhythm, dystrophic changes in the myocardium and fatty degeneration, cirrhosis and atrophy of the liver. It also impairs metabolism, in particular the carbohydrate metabolism and causes persistent hyperglycemia. Because of its toxic properties, chloroform today finds only limited application as an anesthetic; it is chiefly used as an external agent for rubbing into the skin (usually mixed with turpentine, henbane oil or other substances). Chloroform is sometimes prescribed orally in small doses (3—5 drops) in vomiting, pain in the stomach and hiccoughs. It is also used in the form of chloroform water (Aqua chloroformi) containing 0.5% chloroform, 1 tablespoonful 3—4 times a day.

Chloroform is likewise an ingredient of the so-called "anti-smoke mixture" used to reduce irritation of the respiratory passages in cases of poisoning with arsines.

Maximal doses (orally) for adults: single — 0.5 ml daily — 1 ml

To be stored in stoppered bottles of amber glass in a cool place observing safety precautions (List B) Anesthetic chloroform is supplied in special bottles of 50 ml Maximal storage period 6 months For anesthesia only chloroform from bottles opened immediately before the operation can be used

ETHYL CHLORIDE (*Aethylum chloratum* *Aethylus chloridum*) C_2H_5Cl

Synonyms Aether chloratus Chelen Chlorene Chloroetan Kelene

Transparent colourless volatile liquid with characteristic odour Sparingly soluble in water (approx 1:50) Miscible with alcohol and ether Highly flammable when ignited burns with a green flame Specific gravity 0.921–0.923 Boiling point 12–13°

In its resorptive action ethyl chloride is similar to chloroform and ether Anesthesia develops rapidly—within 1–2 minutes the stage of excitement is short The drug is quickly expired by the lungs and consciousness is regained within 2–3 minutes after the end of anesthesia

The lengthy action of ethyl chloride can cause lesions of the parenchymatous organs (especially the liver heart and kidneys) it is therefore used only for basal or temporary anesthesia ("Rauschmarkose")

Ethyl chloride is sometimes used for local anesthesia When it comes in contact with the skin it quickly evaporates thus cooling the skin and lowering sensitivity This makes it possible to perform minor superficial operations It has been reported that spraying the skin with ethyl chloride is effective in the treatment of erysipelas An ethyl chloride "block" has also been proposed for the treatment of neuromyositis neuralgia and other diseases of the muscles and peripheral nerves The possibility of injuring the tissue by cooling too strongly must be kept in mind patients must be prevented from inhaling ethyl chloride that evaporates from the skin

In children under 10 years old a heightened sensitivity to ethyl chloride is often observed for that reason the drug should not be used for anesthesia up to that age

Ethyl chloride is supplied in sealed bottles and in 30 ml ampoules

To be stored in a cool place protected from light observing safety precautions (List B)

NITROUS OXIDE (*Nitrogenium oxydulatum*) N_2O

Synonyms Laughing gas Dinitrogen oxide Oxydum nitrosum Protoxyde d'Azote Stickoxydul

Colourless gas with characteristic odour and sweetish taste Specific gravity—1.527 boiling point—88.7° Is condensed into a colourless liquid at 0° and 30 atmospheres pressure Not inflammable but supports combustion May explode when mixed with ether

Inhaling the pure gas quickly causes anesthesia and asphyxia When mixed with oxygen and administered in the correct dosage it causes anesthesia without initial excitement or side effects Does not irritate the respiratory passages

Nitrous oxide undergoes practically no change in the body it does not combine with the hemoglobin but is dissolved in the plasma After cessation of inhalation it is quickly eliminated from the body through the respiratory passages (within 2–3 min) consciousness is quickly regained and the narcotic condition passes away completely

Nitrous oxide is used for inhalation anesthesia in surgical practice and also for alleviating pain in childbirth it finds application in surgical stomatology Used mixed with oxygen (80% nitrous oxide and 20% oxygen) by means of special apparatus for gas anesthesia and usually preceded by basal anesthesia (intravenous injection of thiopental sodium or hexobarbital sodium)

In nitrous oxide anesthesia the degree of relaxation of the skeletal muscles is usually insufficient to achieve full muscular relaxation additional injections of curarelike drugs are given (see p 122)

Nitrous oxide is supplied in steel cylinders in the liquid state

B Hypnotics and anesthetics derived from barbituric acid and other heterocyclic compounds

Barbituric acid or malonylurea is the basic chemical structure of numerous modern hypnotics and anesthetics



Barbituric acid itself has no hypnotic action it is its derivatives obtained by replacing the hydrogens in position 5 by various organic radicals that possess this ability

Replacing the oxygen bound to the carbon in position 2 by sulphur gives the so called "thio-barbiturates". In some barbiturates the hydrogen joined to nitrogen in position 1 or 3 is replaced by the methyl radical.

The derivatives of barbituric acid are only sparingly soluble in water but their sodium salts have good solubility.

Barbiturates have a depressing effect on the central nervous system and are used in medical practice as sedatives, hypnotics, antispasmodics and anesthetics.

The hypnotic action of barbiturates is associated with their ability to cause an irradiation of the inhibitory process in the cerebral cortex. In large doses the excitatory processes are lowered.

Along with the influence on the cerebral cortex that on the brain stem is also very marked.

Different barbiturates exert an action of varying duration; this is associated with the peculiarities of their transformation in the body and their elimination (see table on page 7).

Barbiturates can be administered per os, intramuscularly, intravenously and rectally. The choice of barbiturate and the method of administration depends on the indications. For a hypnotic or sedative effect they are usually prescribed orally; if the patient falls asleep easily but awakens too soon, a drug with a lengthy action is used; but if he only has trouble in falling asleep, a short acting drug is administered.

Barbiturates are prescribed in enemas for excited patients and for basal anesthesia. Intramuscular administration gives a more rapid effect. Intravenous administration is mainly used for anesthetic purposes.

Long acting barbiturates are mostly excreted through the kidneys; barbiturates with a transitory action are for the most part decomposed in the liver.

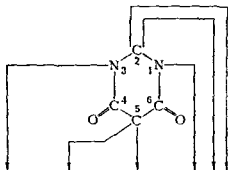
In cases of liver disease the decomposition takes place more slowly and the action of the drugs is prolonged and intensified. For that reason the prescription of barbiturates in cases of liver disease (particularly short acting barbiturates) is contraindicated in diseases of the kidneys; barbiturates with a lengthy period of action should not be prescribed.

The influence of barbiturates on respiration and the circulation depends on the dose, the method and speed of administration. After the usual doses respiration is retarded and the blood pressure falls as a result of the general sedative action. Large doses may cause depressed respiration, vascular collapse, retarded pulse, lowered temperature, oliguria and coma. Rapid intravenous administration may lead to a stoppage of respiration and a sharp fall in the arterial pressure. It must be borne in mind that opiates potentiate barbiturates. Basic metabolism diminishes under the influence of barbiturates; the body temperature falls slightly.

Lengthy use of barbiturates may lead to the development of drug tolerance and habituation

In isolated cases, hypersensitivity to barbiturates is observed as well as an atypical reaction uneasiness and excitement There may be cases of allergic cuti reactions (more often after taking barbitol or phenobarbital)

When barbiturates are used for relieving pain in childbirth it is necessary to take into account the fact that they penetrate the placental barrier quite easily and can also enter the milk of nursing mothers



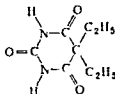
Drug	Substituent in position					Action	Fate in body
	3	5'	5	1	2		
Barbital	H	Ethyl	Ethyl	H	O	Lengthy	Slowly excreted in urine
Barbital sodium	H	Ethyl	Ethyl	Na	O	Ditto	Ditto
Phenobarbital	H	Phenyl	Ethyl	H	O	Ditto	Ditto
Amobarbital sodium	H	Ethyl	Isoamyl	Na	O	Intermediate	Decomposes
Phenobarbital sodium	H	Ethyl	Methylbutyl	Na	O	Ditto	Ditto
Barotal	H	Ethyl	Crotyl	H	O	Ditto	Ditto
Quietal	H	Bromal-lyl	Isopropyl	H	O	Short	Ditto
Hexobarbital sodium	CH ₃	Methyl	Cyclohexenyl	Na	O	Very short	Decomposes
Thiopental sodium	H	Ethyl	Methylbutyl	Na	S	Ditto	Ditto

In search of hypnotics free from the side effects of the barbiturates derivatives of other heterocyclic compounds such as pyridine and piperidine have been synthesized. In the USSR the use of tetrindine a pyridine derivative and methiprylon a piperidine derivative has been permitted. In the Hungarian Peoples Republic a drug called noxiron is being produced — it is a derivative of piperidine.

a) Hypnotics of the barbituric series

BARBITAL (Barbitalum)

5,5 Diethylbarbituric acid



Synonyms Aethinal Athylbarbital Aivenol Barbaethyl Barbitone Barbitural Barbityl Deba Diemal Dormanol Dormonal Embinal Hypnosfer Hypnogène Malonal Malonurea Sédeval Sedival Sonal Uronal Veronal Versinal

White crystalline powder, odourless, slightly bitter taste, sparingly soluble in cold water (1:170), soluble in boiling water (1:15) and in alcohol, freely soluble in alkaline solutions. Boiling point 189—191°.

Barbital is one of the most important hypnotics of the barbituric series. It is used as a sedative and hypnotic, and induces deep unbroken sleep. When using the drug the slowness with which it is decomposed and excreted must be borne in mind; it should not be prescribed over a lengthy period of time. It is to be recommended that after administering the drug for 3—4 days a break of 1—2 days should be made. Side effects take the form of debility, lassitude, nausea, vomiting, headache ("barbitalism"). Barbital is not used for sleep therapy because of possible cumulative effects. As a hypnotic barbital is prescribed orally in a dosage of 0.25—0.5 g $\frac{1}{2}$ —1 hr before retiring; for better absorption it is drunk down with $\frac{1}{2}$ —1 cup of warm tea. Infants from 4 to 12 months old are given doses of 0.075—0.09 g; children from 2 to 5 years — 0.09—0.15 g; from 6 to 12 — 0.2—0.25 g. As a sedative it is prescribed for adults in a dose of 0.05—0.1 g 1—2 times a day.

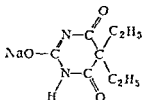
Maximal doses for adults: single — 0.5 g daily — 1.5 g.

Maximal doses for children: Up to 6 months old: single — 0.03 g daily — 0.06 g; from 6 months to 1 year: single — 0.075 g daily — 0.15 g; 2 years: single — 0.1 g daily — 0.2 g; 3—4 years: single — 0.15 g daily — 0.3 g; 5—6 years: single — 0.2 g daily — 0.4 g; 7—9 years: single — 0.25 g daily — 0.5 g; 10—14 years: single — 0.3 g daily — 0.6 g.

Barbital is often prescribed in combination with aminopyrine, antipyrine and bromides. This intensifies the sedative, hypnotic and analgesic effect.

Supplied in powder form and in tablets of 0.25 and 0.5 g. Combined tablets are also available containing 0.1 g barbital and 0.3 g aminopyrine (see Verodir).

To be stored in well stoppered bottles, observing safety precautions (List B).

BARBITAL SODIUM (*Barbitalum natricum*)Sodium 5,5-Diethyl barbiturate (*Natrium diaethylbarbituricum*)

Synonyms Barbitone soluble, Calmine, Diemal *natrium* Embinal *natrium* Medinal, Natrinal, Sombrinal, Soprinal, Veronal sodium

White crystalline powder of bitter taste odourless freely soluble in water (1.5 in cold water and 1.25 in boiling water) sparingly soluble in alcohol insoluble in ether. The aqueous solution is alkaline to phenolphthalein. Solutions for injections are prepared under aseptic conditions.

Barbital sodium as a sedative and hypnotic thanks to its high solubility it acts somewhat more quickly and intensively than barbital. It is also excreted more rapidly and is less toxic.

Used in insomnia nervous excitement and neuralgia and at times as an antiemetic and antispasmodic. Prescribed orally for adults in a dosage of 0.3, 0.5 or 0.75 g, and for children in a dosage of 0.02–0.3 g depending on the age. As a hypnotic it is taken an hour before retiring, it is drunk down with warm tea.

Maximal doses for adults single — 0.75 g daily — 15 g

Maximal doses for children the same as for barbital

Subcutaneously and intramuscularly adults are administered 5 ml of 10% solution (0.5 g barbital sodium) with the addition of 0.005 g procaine hydrochloride. It is also administered in enemas (in 5–15 ml of water) and in the form of suppositories containing 0.5 g.

Supplied in powder form and in tablets of 0.3 g. To be stored in stoppered glass bottles observing safety precautions (List B).

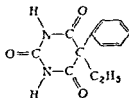
Rp *Barbitali natrici* 0.3

D t d N 6 in tabul

S. 1–2 tables with cup of warm tea an hour before retiring

PHENOBARBITAL (*Phenobarbitalum*)

5-Phenyl-5-ethylbarbituric acid



Synonyms Adonal, Aephenal, Barbeyl, Barbinal, Barbiphen, Barbyphen, Cardenal, Dorminal, Dormital, Duneryl, Fenemal, Gardenal, Leonal, Lepinal, Luminal, Neurobarb, Nunol, Phenemal, Phenobarbitone, Phenonyl, Sedonal, Seveal, Solvinal, Somonal, Zadonal

White crystalline powder of slightly bitter taste, odourless, practically insoluble in cold water, sparingly soluble in boiling water (1:40), freely soluble in alcohol and alkaline solutions. Melting point 174–177°.

Phenobarbital has a sedative hypnotic and antispasmodic effect. As compared with other barbiturates it has a stronger action in lowering the excitability of the motor centres of the brain, and for that reason finds extensive application in the treatment of epilepsy, chorea and spastic paralysis. In small doses it

has a favourable influence in the initial stages of hypertensive disease and in vascular spasm (migraine and stenocardia)

In spasm of the smooth muscles phenobarbital can be used in combination with belladonna preparations papaverine and other spasmolytics As a hypnotic it is prescribed orally for adults in doses of 0.1—0.2 g (sleep ensues in 1—1½ hrs and lasts 6—8 hrs) Children from 4 to 12 months old are given 0.005—0.01 g from 2 to 5 years — 0.02—0.03 g from 6 to 12—0.04—0.075 g

In the treatment of epilepsy phenobarbital is prescribed in an initial dosage of 0.05 g twice daily (for adults) gradually increasing the dose until seizures stop but not administering more than 0.6 g per day Treatment is lengthy In epilepsy administration of phenobarbital should be discontinued slowly since the abrupt withdrawal of the drug may bring on attacks and even status epilepticus Treatment with phenobarbital can be combined with the administration of bromides hexamidine diphenylhydantoin (see pp 61 f2) or other antispasmodics In order to reduce the hypnotic effect caffeine can be given simultaneously It has been reported that in such cases the administration of small doses of phenamine (0.005 g) is advisable

As a sedative and spasmolytic phenobarbital is prescribed in a dosage of 0.01—0.03 g 2—3 times daily

During lengthy use of phenobarbital side effects are observed rather frequently such as ataxia lowering of the blood pressure lassitude and skin rashes

Maximal doses for adults single — 0.3 g daily — 0.6 g

Maximal doses for children Up to 6 months old single dose — 0.005 g daily dose — 0.01 g from 6 months to 1 year single — 0.01 g daily — 0.02 g 2 years single — 0.02 g daily — 0.04 g 3—4 years single — 0.3 g daily — 0.05 g 5—6 years single — 0.04 g daily — 0.08 g 7—9 years single — 0.05 g daily — 0.1 g 10—14 years single — 0.075 g daily — 0.15 g

Supplied in powder form and in tablets of 0.05 and 0.1 g Combined tablets are also available containing

a) phenobarbital 0.05 g papaverine 0.02 g b) phenobarbital 0.2 g papaverine 0.02 g and salsoline 0.03 g c) phenobarbital 0.05 g and salsoline 0.02 g (or 0.03 g) d) phenobarbital 0.1 g and aminopyrine 0.25 g e) phenobarbital dibazol and salsoline 0.025 g each f) phenobarbital 0.02 g (or 0.03 g) and theobromine 0.25 g g) phenobarbital and papaverine 0.02 g each theobromine 0.25 g h) phenobarbital and salsoline 0.02 g each theobromine 0.25 g i) phenobarbital and salsoline 0.03 g each aminopyrine 0.3 g theobromine 0.15 g j) phenobarbital salsoline and papaverine 0.03 g each theobromine 0.25 g

Stored in tightly stoppered bottles of amber glass observing safety precautions (List B)

Karmanova Tablets

Dr Y. I. Karmanova has proposed tablets (or pills) of the following composition for the treatment of epilepsy

Phenobarbitali 0.1

Natrii bromati 0.133

Codeini 0.01

Strychnini nitrati 0.001

Camphorae tritae 0.017

Calcii glycerophosphorici 0.4

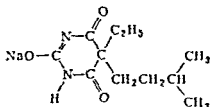
Pulv. et extr. rad. Valerianae 0.042

Besides these tablets (Tablets No. 1) or the corresponding pills each of which contains 0.1 g of phenobarbital Tablets No. 2 are used They contain 0.05 g of phenobarbital and the same doses of the other ingredients as Tablets No. 1

Treatment is carried out in several courses the length and number depending on the severity of the disease and the effectiveness of the remedy

Tablets are stored in tightly stoppered bottles protected from light since they contain strychnine they are kept locked (List A)

AMOBARBITAL SODIUM (*Amobarbitalum natricum*)
Sodium 5-ethyl-5-isoamylbarbiturate



Synonyms Altitinal, Amital, Amylobarbitone sodium Amytal sodium, Barbamyl, Dorlotin, Dorminal, Eunoctal, Hypnamil Isornyl, Sedal

White amorphous powder, odourless, freely soluble in water and alcohol. Solutions for injections are prepared under aseptic conditions, they decompose on boiling.

Has a hypnotic, and in higher doses, an anesthetic effect. Sleep ensues quickly and lasts 6–8 hrs.

Used as a hypnotic in various forms of insomnia and for sleep therapy, also used as a sedative and antispasmodic.

In insomnia amobarbital sodium is administered orally before retiring in a dosage of 0.1–0.2 g for adults; children are given up to 0.01 g for each year of life. The drug is sometimes prescribed in enemas or in suppositories (0.3–0.5 g for adults).

As an antispasmodic and in cases of mental excitement amobarbital sodium is administered intramuscularly in doses of 5–10 ml of 5% solution. In acute mental excitement 5–8 ml of 5–10% solution are sometimes administered intravenously, intravenous administration should be slow (not more than 1 ml per min).

Like other barbiturates amobarbital sodium potentiates local anesthetics; it can be used to intensify local anesthesia during surgical operations. As a sedative and antispasmodic amobarbital sodium can be prescribed in a dosage of 0.025–0.05 g 2–3 times a day, in combination with papaverine, belladonna preparations, etc. It has been reported that amobarbital sodium is effective in coronary atherosclerosis, use of the drug leads to a reduction of the cholesterol content of the blood, an increase in the lecithin content and an abatement of pain, while seizures of stenocardia occur less frequently or cease altogether (L. A. Myasnikov).

In sleep therapy amobarbital sodium is prescribed orally in a dosage of 0.1, 0.2 or 0.3 g 3–4 times a day (but not in excess of the maximal daily dose). Sleep lasts 16–20 hrs a day. The duration of treatment is from 12 to 14 days or more, depending on the indications. When the drug is used over lengthy periods of time a careful watch must be kept over the condition of the cardiovascular system and the function of the liver and the hemopoietic system.

Maximal doses for adults: single—0.5 g daily—1 g.

Maximal doses for children up to 6 months old: single—0.01 g daily—0.02 g, from 6 months to 1 year: single—0.01 g daily—0.02 g, 2 years: single—0.02 g, daily—0.04 g, 3–4 years: single—0.03–0.04 g daily, 0.06–0.08 g, 5–6 years: single—0.05 g daily—0.1 g, 7–9 years: single—0.07–0.1 g daily—0.15–0.2 g, 10–14 years: single—0.15–0.2 g daily—0.3–0.4 g.

Available in powder form and in tablets of 0.1 and 0.2 g.

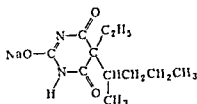
To be stored in well stoppered bottles, observing safety precautions (List B).

Rp Amobarbitali natrici 0.1 (0.2)

D t d. N 6 in tabul

S 1 tablet before retiring

PENTOBARBITAL SODIUM (*Pentobarbitalum natricum*)
Sodium 5 ethyl 5 (1 methylbutyl) barbiturate



Synonyms Aethaminalum Natrium, Embutal, Ethaminal sodium, Euthatal, Isobarb, Mebubarbital, Napental, Narcoren, Nembutal, Nembutal sodium, Pental, Pentobarbital soluble, Pentodorm, Pentone, Prodormol, Somno, pentyl, Sopenal.

White crystalline powder, odourless, bitter taste, soluble in water and alcohol, insoluble in ether. Aqueous solutions have an alkaline reaction, decompose on standing and when boiled.

Pentobarbital sodium can be considered an isomer of Amobarbital sodium. The two drugs have the same empirical formula ($C_{11}H_{17}O_3N_2Na$), and differ only in the position of the methyl group in the side chain: in amobarbital it is in the γ position and in pentobarbital it is in the α position.

In its action, pentobarbital sodium is also similar to amobarbital sodium; it decomposes, however, somewhat more rapidly and its action is somewhat shorter in some cases; it is tolerated better.

Pentobarbital sodium is prescribed orally; the usual hypnotic dose for adults is 0.1–0.2 g. In sleep therapy it is administered in a dosage of 0.1–0.2 g 3–4 times daily. It can also be administered rectally (in suppositories and enemas containing 0.2–0.3 g). Intravenously it is injected slowly in the form of a fresh aseptically prepared 5% solution (5–10 ml).

Maximum doses for adults: single dose — 0.5 g, daily dose — 1 g.

Available in powder form and in tablets of 0.1 g.

To be stored in well stoppered bottles of amber glass, observing safety precautions (List B).

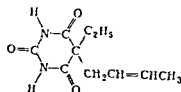
Rp Pentobarbitali natrici 0.1

D t d N 6 in tabul

S 1 tablet half an hour before retiring

BAROTAL (*Barotalum*)

5 Crotyl 5 ethyl barbituric acid



Synonym Kalypnon

White crystalline powder, odourless, bitter taste. Sparingly soluble in water, freely soluble in alcohol, ether and alkaline solutions. Melting point 110–115°.

Like other barbiturates, barotal acts as a sedative and hypnotic. After a single administration, sleep lasts 6–8 hrs. Used in cases of nervous excitement, neuralgia and insomnia. May also be used to potentiate antispasmodics. Single dose for adults 0.125–0.25 g.

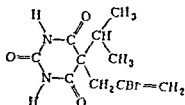
Maximal doses for adults single dose—0.5 g, daily dose—1 g

Available in powder form and in tablets of 0.25 g

To be stored in well stoppered bottles in a place protected from light observing safety precautions (List B).

QUIETAL (Quietalum)

5 Isopropyl 5 bromallyl barbituric acid



Synonyms Noctal, Noctenal, Nostal, Propaldon, Propallylonal

White crystalline powder, odourless, bitter taste, sparingly soluble in water freely soluble in alcohol Melting point 179—185°.

Hypnotic, prescribed orally for adults in dosage of 0.1—0.3 g, in powders or tablets Sleep ensues in 1/2—1 hr after administration

The action of quietal is less prolonged than that of other barbiturates After a single dose sleep usually lasts 3—4 hrs

Available in powder form and in tablets of 0.1 g

To be stored in bottles of amber glass, observing safety precautions (List B)

b) Hypnotics derived from pyridine and piperidine

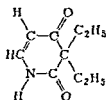
TETRIDINE (Tetridinum)

2,4 Dioxo 3,3 diethyl tetrahydropyridine

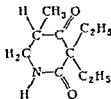
Synonyms Benedorm, Persedon, Presidon, Pyridion, Pyrithyldion

White crystalline powder, soluble in water (1 : 100) and in organic solvents Melting point 97—98°

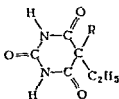
In its chemical structure tetridine is close to methyprypton (p 14), both drugs are structurally somewhat similar to the barbiturates but the difference in the heterocyclic systems on which they are based influences the intensity of the hypnotic effect and the extent to which they are tolerated



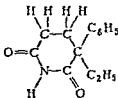
Tetridine



Methyprypton



Barbitals $R = C_6H_5$
Phenobarbital. $R = C_6H_5$



Noxiron

Tetridine acts as a sedative and hypnotic only slightly toxic in hypnotic doses has no significant influence on respiration and circulation Sleep induced by tetridine closely resembles natural sleep and is not so deep as after the administration of barbiturates Sleep ensues in 20—30 minutes after administration of the drug and lasts 5—7 hours

Tetridine is prescribed orally in various forms of insomnia the effect is more constant in cases of insomnia caused by functional disorders of the central nervous system the drug is less effective in organic diseases Can be prescribed in combination with barbiturates and other hypnotics Single dose for adults — 0.2—0.3 or 0.4 g In sleep therapy can be used in the same doses 2—3 times a day

Maximal doses for adults single — 0.5 g daily — 1.5 g

Side effects (nausea vomiting weakness vertigo headache) are seldom observed

Available in powder form and in tablets of 0.1 and 0.2 g

To be stored in tightly stoppered bottles in a place protected from light observing safety precautions (List B)

METHYPRYLON (Methypylonum)

2.4-Dioxo-3,3-diethyl-5-methyl-piperidine

Synonyms Dimerine Noludar

In chemical structure methypylon differs from tetridine in not having a double bond in the nucleus and in the presence of a methyl group in position 5 (see formula on p. 13)

White crystalline powder freely soluble in water and in organic solvents Melting point 74—75°

Methypylon has a pronounced sedative and hypnotic effect only slightly toxic Somewhat more active than tetridine Sleep ensues in 20—30 min after administration and continues 5—7 hrs Doses for adults as a sedative — 0.05—0.1 g 3—4 times a day as a hypnotic — 0.1—0.2 g (less frequently up to 0.3—0.4 g) The drug is usually tolerated well In rare cases there is headache and a feeling of lassitude

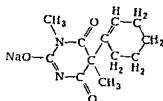
Available in powder form and in tablets of 0.05—0.1 and 0.2 g

To be stored in closely stoppered bottles in a place protected from light observing safety precautions (List B)

c) Barbiturates used for intravenous anesthesia

HEXOBARBITAL SODIUM (Hexobarbitalum natricum)

Sodium 5 (1-cyclohexenyl) 1,5-dimethyl barbiturate



Synonyms Cyclobarbitalum solubile Cyclonal Cyclural Dorico Endodorm Enhexymal natrium Enmal natrium Eudorm Evipal soluble Evipan sodium Hexanastab Hexenal Hexobarb tone soluble Methexenyl Methylhexabarbital soluble Methylhexobital Narconat Narcosanum solubile Noctuvane Novopan Privenal Tobinal

White or slightly yellowish powder or foamy mass deliquesces on exposure to air, faintly bitter taste decomposed by carbon dioxide of air. Freely soluble in water and alcohol insoluble in ether. Aqueous solutions of hexobarbital sodium are unstable they hydrolyze easily and decompose on sterilization. Solutions are prepared under aseptic conditions immediately before use. Solutions can be kept for a maximum of one hour. Only absolutely transparent solutions are fit for use.

Hexobarbital sodium acts as a hypnotic and in large doses as an anesthetic. The drug is chiefly used for intravenous anesthesia but can also be used as a sedative in cases of motor excitement and as an antispasmodic.

Hexobarbital sodium is administered intravenously and at times intramuscularly or rectally. Solutions are prepared immediately before use. The vial is opened and 10 ml of twice distilled water or of sterile isotonic saline warmed to body temperature is added by means of a sterile syringe. The solution is injected slowly into the vein at a rate of not more than 1 ml per min. It must be borne in mind that when hexobarbital sodium (like other barbiturates) is administered intravenously the toxic effects are enhanced if the rate is increased. The dosage should be individualized. For intravenous anesthesia from 2 to 10 ml of 10% solution are administered, depending on the patient's age and condition. For intramuscular administration the dosage is 3–10 ml of 10% solution. When administered intravenously the doses indicated induce transitory anesthesia (20–30 min). For basal anesthesia a 2–25% solution is used. Usually 4–6 ml of 2.5% solution are injected over a period of 10–15 sec. Then after waiting 30–35 sec an additional administration is given. Ordinarily a maximum of 0.5 g of the drug is used. In order to obtain a more prolonged anesthesia hexobarbital sodium is sometimes administered in divided doses. 3–5 ml of 10% solution are first injected and then as the patient begins to recover consciousness the same dose is repeated. When the drip method is used the drug is infused in the form of a 2% solution in isotonic saline at a rate of 10–20 drops per min. later the number of drops is reduced to 5–10 per min.

Hexobarbital anesthesia can be combined with inhalation anesthesia or local anesthesia. For basal anesthesia it can be administered in enemas. To overcome excitement hexobarbital is administered intravenously in a dose of 2–10 ml of 10% solution depending on the patient's condition.

Maximal single dose intravenously (for adults) — 1 g (10 ml of 10% solution or 40 ml of 25% solution).

Hexobarbital sodium is contraindicated in cases of impaired liver or kidney function, sepsis, cachexia, shock, collapse, inflammatory diseases of the throat and nasopharynx, fever and oxygen deficiency. In cases of ileus the use of hexobarbital anesthesia is not recommended since it inhibits the motor activity of the intestine.

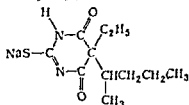
When hexobarbital sodium is administered too rapidly depressed respiration and impaired cardiac activity may develop. If there should be complications artificial respiration is started and the patient is made to inhale oxygen or a mixture of oxygen and carbon dioxide. ephedrine, caffeine, sodium benzoate, pentylenetetrazol or nikethamide and cytolon are administered.

Available in hermetically sealed vials or ampoules containing 1 g of the dry drug.

To be stored in hermetically sealed vials in a cool dry place protected from light observing safety precautions (List B).

Rp Hexobarbitali natrici 10
D t d N 3 in amp
S For intravenous anesthesia

THIOPENTAL-SODIUM (Thiopentalum natrium)
Sodium 5 ethyl 5 (1 methylbutyl) 2 thiobarbiturate



Synonyms Farmotal Intraval Leopental Nesdonal Penthiobarbital Pen-
tothal sodium Pharmotal Thiomebumal sodium Thionembulal Thiopentalum
natrium Thiopenten Thiopentobarbital Thiopentone sodium Thiotat natrium
Ticpan Trapanal

Dry greenish yellow porous mass or yellowish white powder. Freely soluble
in water, hygroscopic. Aqueous solutions have an alkaline reaction.

Thiopental sodium solutions are unstable and are therefore prepared under
aseptic conditions immediately before use; they are not sterilized.

Thiopental sodium acts as a hypnotic, and in large doses as an anesthetic.
Chiefly used for intravenous anesthesia. The effect is very similar to that of
hexobarbital sodium, but thiopental sodium is more potent and is quicker acting.
It induces a more pronounced muscular relaxation than hexobarbital sodium, but
can nevertheless cause laryngospasm, proluse secretion and other symptoms of
vagotonia — something that is not observed when hexobarbital sodium is admi-
nistered. Thiopental sodium is quickly decomposed and excreted. Anesthesia
after the administration of a single dose of the drug lasts 20–25 min.

Thiopental sodium must be injected into the vein slowly — not more than
1 ml of solution per min; otherwise there is a danger of collapse.

For anesthesia 1.25% or 2.5% solutions are used; they are prepared imme-
diately before use. In order to prepare a 2.5% solution 40 ml of freshly boiled
sterile twice distilled water is added to 1 g of thiopental sodium. Only absolu-
tely transparent solutions are fit for use.

Thiopental sodium is usually injected into the cubital vein. 4–6 ml of 2.5%
solution (0.1–0.15 g of the drug) is injected in 10–15 sec, after an interval of
30 sec an additional 4–8 ml is injected in 1–3 min. In minor operations when
thiopental sodium alone is used a total of 14–25 ml of 2.5% solution is admi-
nistered (0.35–0.625 g of the drug). For basal anesthesia up to 2 ml is injected
during the first 15 sec, and 30–40 sec later an additional amount is injected.
For an adult 8–12 ml of 2.5% solution is usually sufficient.

Children are given intravenous injections of a 2% solution at a rate of 0.5–
1 ml per year of age for the entire operation. Administration is slow with inter-
vals gradually deepening the anesthesia. Children may also be given a rectal
administration of a warm 5% solution of thiopental sodium (at a temperature
of 32–35°) the dose being calculated at a rate of 0.04 g per year of age up to
3 years and 0.05 g per year of age from 3 to 7 years.

Maximal single intravenous dose for adults — 1 g (40 ml of
2.5% solution).

At the end of anesthesia the patient usually regains consciousness in 10–
15 min but the somnolent condition continues for several hours.

Thiopental sodium is contraindicated in diseases of the liver and kidneys,
diabetes, emaciation, shock, collapse, bronchial asthma, inflammatory diseases
of the throat and nasopharynx, oxygen deficiency and fever. Possible complica-
tions: depressed respiration and circulation. In such cases oxygen is given and
ephedrine, pentylenetetrazol or nikethamide and cyllon are administered intra-
venously or intramuscularly.

Available in hermetically sealed vials or ampoules containing 1 g thiopen-
tal sodium and 0.06 g anhydrous sodium carbonate which acts as a buffer.

To be stored in hermetically sealed vials in a cool dry place, protected from light observing safety precautions (List B)

Rp Thiopentali natru 10
D t d N 3 in amp
S For intravenous anesthesia

C. Hypnotics and anesthetics of the aliphatic series

CHLORALHYDRATE (Chloralum hydratum Chlorali hydras)



Synonyms Chloraldurat, Lorinal, Orphofarm, Somnos

Colourless transparent crystals or fine crystalline powder with characteristic pungent odour and slightly bitterish, acrid taste, freely soluble in water, alcohol ether and chloroform

Deliquesces in the air and slowly evaporates Incompatible with alkalis, liquefies when mixed with camphor, antipyrine or menthol

Sedative, hypnotic and analgesic, in large doses approaching the toxic, has anesthetic properties Has a complicated influence on the central nervous system in small doses causes a weakening of the inhibitory process, but in large doses lowers the excitatory processes, toxic doses strongly depress the excitability of the nerve cells

Prescribed as a sedative in dosage of 0.2–0.5 g and as a hypnotic in dosage of 0.5–1 g (for adults) Also used in cases of mental excitement and as an antispasmodic in spasmophilia, tetanus, eclampsia, etc

Infants from 4–12 months old are prescribed doses of 0.05–0.15 g, children from 2–5 years – 0.15–0.2 g and from 6–12 years – 0.25–0.4 g

Also administered orally and in enemas diluted with demulcents (because of the drug's irritating effect on the mucosa of the stomach and intestine) Chloral hydrate is quickly absorbed Sleep ensues within 15–20 min and continues 6–8 hrs, often being accompanied by an undesirable fall in the arterial pressure

Maximal doses for adults single – 2 g, daily – 6 g

Maximal doses for children up to 6 months old single – 0.1 g daily – 0.3 g, from 6 months to 1 year single – 0.15 g daily – 0.45 g, 2 years single – 0.15 g, daily – 0.45 g; 3–4 years single – 0.2 g, daily – 0.6 g 5–6 years single – 0.25 g, daily – 0.75 g, 7–9 years single – 0.3 g, daily – 0.9 g, 10–14 years single – 0.3–0.5 g, daily – 0.9–1.5 g

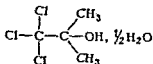
Contraindicated in marked diseases of the cardiovascular system, liver and kidneys

Available in powder form and in tablets of 0.5, 0.75 and 1.5 g

To be stored in well stoppered bottles in a cool place protected from light observing safety precautions (List B)

CHLOROBUTANOL (Chlorobutanolum)

1,1,1 Trichlor 2 methyl 2 propanol



Synonyms Acetorchloroform Anesthosal Ancon Chlorbutol Chloretone Clortran Methaform Sedaform

Colourless crystals with odour of camphor sparingly soluble in water (1:250) freely soluble in alcohol ether, chloroform and fatty oils Melting point $-77^{\circ}-80^{\circ}$

Chlorbutanol has a general sedative and mild anesthetic effect Also has local anesthetic and antiseptic properties

Influence on the central nervous system is very similar to that of chloral hydrate In anesthetic doses can cause a depression of respiration and a lowering of the arterial pressure

Chlorobutanol is prescribed orally as a sedative and antileptic in a dosage of 0.3–0.5 g and as a hypnotic in a dosage of 0.5–1 g Can be administered in the same doses in enemas and suppositories

Externally the drug is used in treating ulcers wounds and inflammatory processes in the form of a 1–2% dusting powder, a 5–10% ointment or a 0.4% lotion

In the pharmaceutical industry chlorobutanol is used as a preservative for galenics and other preparations (gitalin adrenalin and organo preparations)

To be stored in well stoppered glass bottles in a cool place protected from light

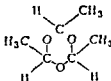
Chlorobutanol inhalant (Chlorobutanolum pro Inhalatione)

A solution of chlorobutanol (0.5 g), camphor (0.625 g) and menthol (0.625 g) in liquid petrolatum (25 ml)

Used as an antiseptic and anesthetic for inhalation or for introducing into the nose by pipette in diseases of the nasopharynx and larynx (rhinitis pharyngitis laryngitis etc) 2–3 drops in each nostril also used for rubbing into the skin in cases of pruritus

Available in vials of 2.5 ml

PARALDEHYDE (Paraldehydum)

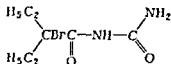


Synonym Paracetaldehyde

Colourless transparent liquid of characteristic odour neutral or slightly acid reaction soluble in water Miscible with alcohol and ether in all proportions flammable Specific gravity—0.998–1.003 Boiling point $120^{\circ}-123^{\circ}$ on cooling solidifies forming crystals with a melting point of $10^{\circ}-11^{\circ}$ Under the influence of air and light and on long standing decomposes with the formation of acetic acid The use of partially decomposed paraldehyde is dangerous in enemas it may cause burns on the mucous membrane of the rectum

Paraldehyde is a sedative and hypnotic Its action is similar to that of chloral hydrate but it is less toxic Paraldehyde is quickly absorbed sleep ensues in 15–30 minutes after administration and after the usual dose of 3–5 ml for adults

CARBROMAL (Carbromalum)
Bromodiethylacetylurea



Synonyms Adabrom, Adalin, Adormin, Beridormin Brevisomnol Bromadal, Carbadal, Carbamidum bromdiethylaceticum, Diacid, Isobroval, Nyctal Optodorm, Persomnin, Planadaln Somben Uradal, Zoridorm

White crystalline powder with very faint odour, practically insoluble in cold water, sparingly soluble in hot water, soluble in alcohol Melting point 116—119°

Carbromal acts as a sedative and mild somnifacient Hypnotic doses cause no disorders in the general condition, respiration or circulation Quickly eliminated from the body, cumulative effect is not observed

Used as a sedative in *neurasthenia hysteria* and various diseases of the nervous system, as well as in preparation for operations and as a hypnotic when patients have difficulty in falling asleep and when sleep is too light

Carbromal is prescribed orally in the following doses as a sedative — 0.2—0.3 g 2—3 times a day, as a hypnotic — a single dose of 0.5—0.75 g an hour before retiring For better absorption and quicker action it is recommended that the drug should be drunk down with half a cup of weak warm tea

Maximal doses for adults single — 1 g, daily — 2 g

Maximal doses for children from 6 months to 1 year old, single — 0.1 g, daily — 0.2 g; 2 years single — 0.15 g, daily — 0.3 g, 3—6 years single — 0.2 g, daily — 0.4 g 7—9 years single — 0.25 g daily — 0.5 g, 10—14 years single — 0.3 g, daily — 0.6 g Infants up to 6 months old are not prescribed carbromal

Contraindicated in cases of hypersensitivity to bromine

Available in powder form and in tablets of 0.3 and 0.5 g

To be stored in bottles of amber glass or in glass tubes observing safety precautions (List B)

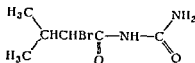
Rp Carbromali 0.5

D t d N 10 in tabul

S 1 tablet an hour before retiring (to be drunk down with half a cup of warm tea)

BROMISOVALUM

α Monobromisovalerylurea or α bromisovalerylcabamide



Synonyms Abroval, Albroman, Alluval, Alural, Bromodorm, Bromural Bromuresan, Bromyl, Brovarin, Carbamidum bromisovalerylicum, Dormigene Isobromyl, Isonaurin, Isoval, Leunerval, Sedural, Somnibrom, Somnurol, Uvaleral, Valinil, Valueua, Verobroman

White crystalline powder of bitterish taste and faint odour, very sparingly soluble in water (1 450), soluble in alcohol (1 17) Melting point 145—150°

Has a sedative and moderate hypnotic effect Tolerated well, usually causes no symptoms of bromism

Prescribed orally in the following doses as a sedative — 0.2—0.3 g once or twice a day, as a hypnotic — 0.3—0.5 g half an hour before retiring (to be

drunk down with half a cup of sweet warm weak tea]. The hypnotic effect is intensified if aminopyrine is taken simultaneously

Prescribed for children in cases of insomnia, chorea and whooping cough in doses of 0.03—0.1, 0.2 or 0.3 g, depending on the age In whooping cough bromisovalum is often administered along with codeine

Maximal doses for adults single—1 g, daily—2 g

Maximal doses for children up to 6 months old, single—0.05 g, daily—0.1 g, from 6 months to 1 year single—0.1 g daily—0.2 g, 2 years single—0.15 g, daily—0.3 g, 3—4 years single—0.2 g, daily—0.3 g, 5—6 years single—0.25 g, daily—0.4 g, 7—14 years single—0.3 g, daily—0.5 g

Available in powder form and in tablets of 0.3 g

To be stored in closely stoppered bottles or glass tubes observing safety precautions (List B)

Rp Bromisoval 03

D t d N 10 in tabul

S 1 tablet twice a day

TRIBROMOETHANOL (Tribromaethanolum) $\text{CBr}_3 - \text{CH}_2\text{OH}$

Synonyms Avertin Basibrol, Bromethol, Ethabrom, Ethobrome, Narcolan Narcotyl Rectanol Renarcol

Fine white crystalline powder freely soluble in alcohol and ether, less soluble in water Melting point $80-82.5^\circ$ Decomposes under the influence of light Aqueous solutions decompose when heated above 40° with the formation of toxic substances hydrogen bromide and dibromoacetaldehyde

Tribromoethanol is an agent for rectal anesthesia Lately it has not been widely applied but it is sometimes employed for basal anesthesia (in combination with ether, nitrous oxide or other anesthetics) By using tribromoethanol it is possible to put the patient to sleep in the ward, in this way reducing psychic trauma When tribromoethanol is used a marked stage of excitement is not observed The drug is introduced into the rectum in a dose of 0.06—0.09 g per kg of body weight

Maximal single rectal dose for adults is 0.1 g per kg of body weight

Tribromoethanol is used in the form of a 2.5% aqueous solution (less frequently 3.5%), prepared ex tempore The distilled water is preliminarily warmed to $35-38^\circ$ and the tribromoethanol added, when stirred well the drug dissolves in 5—15 min The solution must be tested before use, since tribromoethanol may decompose if overheated while being dissolved The decomposition products have an extremely irritating effect on the mucous membrane of the rectum The test is made in the following way 5 ml of the tribromoethanol solution is poured into a test tube and 1—2 drops of a 0.1% aqueous solution of Congo red added the solution should assume an orange red colour, a violet colour shows that it is unfit for use

Tribromoethanol can also be used in the form of a water alcohol solution For adults the necessary dose of the drug is dissolved in 8—10 ml of ethyl alcohol, for children it is dissolved in 3—5 ml of alcohol Isotonic saline or distilled water is then added (A Z Manevich)

The warm solution is introduced into the rectum to a depth of 10—15 cm over a period of 3—5 min In 3—10 min languor ensues followed by deep sleep without initial excitement The deepest sleep is observed in 25—30 min At that moment anesthesia is enhanced with ether, nitrous oxide or other anesthetics and the operation begun

If there should be complications involving respiration and circulation, lavage of the rectum must be performed in addition to the usual measures

Basal anesthesia with tribromoethanol is used in children (more than 1 year old) in patients with thyrotoxicosis and in cases of exaggerated nervous excitability Independent tribromoethanol anesthesia is sometimes resorted to in

operations on the head and neck when it is difficult to employ inhalation anesthesia

Contraindications to the use of tribromoethanol impaired liver function sepsis shock enteritis colitis cachexia and senility Tribromoethanol anesthesia is not used in infants up to 1 year old

To be stored in bottles of amber glass with ground glass stoppers

II SEDATIVES AND NEUROPLEGIC AGENTS

Medicinal substances that allay excitement are called sedatives By heightening the inhibitory process or by depressing the excitatory process they can have a regulating effect on the central nervous system In ordinary doses they usually do not induce anesthesia or sleep they can however facilitate the onset of natural sleep and intensify it and can potentiate anesthetics and hypnotics etc.

Sedatives include substances of diverse chemical classes In small doses hypnotics usually have a sedative effect The chief sedatives are bromides a group of compounds that was studied in detail by I P Pavlov and his pupils I P Pavlov emphasized that "bromine has a special relation to the inhibitory process which it restores and intensifies (I P Pavlov "Complete Collected Works Moscow Leningrad 1952 v 6 p 436)

Investigations aimed at finding new sedatives have lately been undertaken on a broad scale The success achieved in the pharmacological and clinical study of the phenothiazine derivatives (chlorpromazine and others) and the alkaloid reserpine have stimulated the development of this branch of neuropharmacology Along with the use of many new sedatives a number of new terms have been proposed in the literature to characterize the pharmacological and therapeutic peculiarities of these drugs Some of the terms widely used are neuroplegic neuroleptic and neurolytic substances psychosedatives tranquilizers ataractics antiphobic substances The term "tranquillizer" from the meaning of the word gives the idea of a drug which restores calmness and serenity The term "ataractic" comes from the Greek "ataraxia" meaning tranquillity of spirit or indifference The term "antiphobic" arises from the ability of some drugs to have a tranquillizing effect in pathological conditions accompanied by fright and emotional tension

The term "neuroplegic" meaning an agent blocking the nervous system was first proposed for substances causing a "regulatory inhibition of the neuro autonomic system" and used in artificial sleep induced by cooling the body (hibernation) This is a broader term than "sedative" and implies a many-sided action on the functions of the central and autonomic nervous systems leading to a blocking of the autonomic system to an "economical" state of the body with lowered metabolism relaxation of the muscles and a twilight condition recalling anesthesia (A Labori and P Gugenar) Since the majority of the new sedatives act not only on the central nervous system but also on various elements of neuro reflex regulation and metabolism the term "neuroplegic" can be used conditionally as a general name for these drugs

Attempts have also been made to divide these drugs into classes The Psychiatrists Congress held in Zurich in 1957 proposed that the entire group of neuroplegics should be divided into two groups according to the character of their therapeutic effect a) neuroleptic substances — those mainly used in severe impairment of the activity of the central nervous system (psychoses) and b) tranquillizing substances — those used in less pronounced impairment of the function of the central nervous system for the most part in neuroses with a state of psychic tension and fright According to this classification neuroleptic substances would include chlorpromazine and other phenothiazine derivatives and the alkaloid reserpine tranquillizers would include derivatives of propanolol (meprotan and the like) and derivatives of *d* phenylmethane (amizyl etc.)

This classification has not however been generally accepted. Another proposal (by Alexander) is to divide neuroleptic substances into 3 groups: a) tranquillizers — substances with a strong central depressant action (chlorpromazine, reserpine); b) ataractic and antiphobic substances which reduce psychic tension and a feeling of fright (amizyl etc); and c) central muscular relaxants which reduce psychic and muscular tension (meprotan and its analogues). According to still another classification (Bovet) all "psychotherapeutic" substances called "tranquillizers" are divided into 4 groups: a) neuroleptics which cause a pronounced tranquillizing of the central nervous system (chlorpromazine, reserpine); b) antiphobics which have a mild antidepressive action (amizyl); c) central relaxants which have a stronger tranquillizing action than neuroleptics and do not cause a subsequent depression (meprotan etc); and d) ataractics which improve the neuropsychic equilibrium without having a hypnotic effect.

Because of the ability of chlorpromazine and its analogues and of reserpine and some other drugs to weaken or abolish hallucinations in psychic diseases and in changes in the higher nervous activity caused by so-called "hallucinogenic" substances (diethylamide of lyserginic acid, mescaline etc) proposals have also been made to set up a special group of antihallucinogenic agents.

A Bromides

MONOBROMATED CAMPHOR (Camphora monobromata)

Colourless crystals or white crystalline powder with odour and taste of camphor. Freely soluble in ether (1:2), alcohol (1:9) and chloroform; very sparingly soluble in water.

Like other bromides, monobromated camphor has a sedative effect on the central nervous system, also improves cardiac activity.

Used in cases of heightened nervous excitability, neurasthenia and cardiac neurosis.

Prescribed orally in powders, tablets or pills in a dosage of 0.1–0.5 g for adults 2–3 times a day; children from 2 to 5 years old are prescribed doses of 0.01–0.1 g and from 6 to 12 years old doses of 0.15–0.2 g.

Available in powder form and in tablets of 0.25 g.

To be stored in tightly stoppered bottles of amber glass in a place protected from light.

Bekhterev tablets

Composition: each tablet contains 0.25 g potassium bromide, 0.138 g dry extract of Spring Adonis and 0.006 g codeine (base).

Prescribed in a dosage of 1–2 tablets a day as a sedative. Two tablets are the equivalent of one tablespoonful of the corresponding mixture.

Available in glass vials containing 25 tablets.

B Phenothiazine derivatives

Phenothiazine or thiodiphenylamine is known as an antiseptic and helminthic.

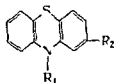


Phenothiazine





In the past it was used in medicine as an anthelmintic in enterobiasis, and as an antiseptic in inflammatory diseases of the urinary tract. Today, due to the introduction of more effective and less toxic drugs, it is no longer used in medical practice. In veterinary science phenothiazine is used in helminth invasions of cattle, swine and horses. Technical (unpurified) phenothiazine is also used to destroy mosquito larvae.

One of the derivatives of phenothiazine is methylene blue.

It was established in 1945 that when the hydrogen joined to the nitrogen atom in the phenothiazine nucleus is replaced by alkylaminoalkyl radicals, compounds can be obtained which have strong antihistaminic and cholinolytic activity, as well as other important pharmacological properties.



Name of drug and principal synonyms	R_1	R_2	Principal forms of pharmacological activity
Fenethazine Etisine Anergen	$\text{CH}_2\text{CH}_2-\text{N}(\text{CH}_3)_2$	H	Antihistaminic
Diprazin Promethazine Phenergan	$\text{CH}_2\text{CH}-\text{N}(\text{CH}_3)_2$ CH_3	H	Strong antihistaminic, moderate sedative and adrenolytic
Diethazine Dinezin Diparcol	$\text{CH}_2\text{CH}_2-\text{N}(\text{C}_2\text{H}_5)_2$	H	Central cholinolytic (active in parkinsonism)
Chlorpromazine Aminazine Largactil	$\text{CH}_2\text{CH}_2\text{CH}_2-\text{N}(\text{CH}_3)_2$	Cl	Strong sedative (neuroplegic) adrenolytic, antiemetic, moderate antihistaminic
Propazine Promazine	$\text{CH}_2\text{CH}_2\text{CH}_2-\text{N}(\text{CH}_3)_2$	H	Similar to aminazine but somewhat less active
Acetazine Acepromazine Plegicil	$\text{CH}_2\text{CH}_2\text{CH}_2-\text{N}(\text{CH}_3)_2$	COCH_3	Similar to aminazine but somewhat more active

Name of drug and principal synonyms	R ₁	R ₂	Principal forms of pharmacological activity
Methopromazine Mopazine Laevopromazin	$\text{CH}_2\text{CH}_2\text{CH}_2-\text{N}(\text{CH}_3)_2$	OCH_3	Similar to aminazine but somewhat less active and less toxic; less frequently induces subsequent depression
Pacatal Mepazine		H	Moderate sedative, antiemetic, cholinolytic and adrenolytic; less toxic than aminazine; does not induce subsequent depression
Prochlorperazine Stemetil Compazine	$(\text{CH}_3)_2-\text{N}$  $\text{N}-\text{CH}_3$	Cl	Similar to aminazine, less frequently induces subsequent depression; less hypotensive effect
Flapyrazine Perphenazine Decantan Trilafon	$(\text{CH}_3)_2-$  $\text{N}-\text{CH}_2\text{CH}_2\text{OH}$	Cl	Similar to aminazine but more active; potent antiemetic
Trifluoroperazine Stelazine	$(\text{CH}_3)_2-\text{N}$  $\text{N}-\text{CH}_3$	CF_3	Strong neuroplegic and antiemetic

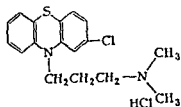
The first alkylamine derivative to find application as an antihistamine was the hydrochloride of 10 (2 dimethylamino ethyl) phenothiazine, the drug known as etisine in the USSR (see p 65). Further investigation showed that the hydrochloride of 10 (2' dimethylaminopropyl) phenothiazine or diprazin (see p 135) had greater antihistaminic activity. As a result of a more detailed study of these and similar derivatives of phenothiazine it was established that they have a pronounced influence on the central and peripheral nervous systems. Along with its antihistaminic activity, diprazin has the ability of potentiating hypnotics, analgesics and general and local anesthetics. It can lower the body temperature, have an antiemetic effect and weaken the action of adrenalin on the body.

In an attempt to find substances having a more active influence on the body functions, derivatives of phenothiazine were synthesized in which chlorine was substituted at position 2 in the nucleus. One of the most potent compounds in this series is the hydrochloride of 2 chloro 10 (3' dimethylaminopropyl) pheno

thiazine or chlorpromazine. This drug has found wide application as a neuroleptic. Subsequently many other derivatives of phenothiazine were synthesized which have a marked neuroleptic effect. In the USSR the following derivatives of phenothiazine have been confirmed for use in medical practice: diprazine, fenethazine, diethazine, chlorpromazine, promazine and mepazine. Other drugs are used abroad including phenothiazine derivatives with the piperazine nucleus in the side chain (R_1). Some of these drugs have now been synthesized in the USSR.

CHLORPROMAZINE (Chlorpromazinum)

2-Chloro-10-(3'-dimethylaminopropyl) phenothiazine hydrochloride



Synonyms: Aminazine, Amliactil, Amplictil, Chlorpromazini hydrochloridum, Contomin, Fenactil, Hibanil, Hibernat, Largactil, Megaphen, Plegomazin, Promactil, Propaphenin, RP 4560, Thorazine, Winteramin.

White or creamy white fine crystalline powder, hygroscopic, very readily soluble in water, alcohol and chloroform; insoluble in ether and benzene. Melting point 194–197°. Powder and aqueous solutions darken under the influence of light. Solutions have an acid reaction; they can be sterilized by holding at 100° for 30 min. Solutions, however, are usually not sterilized as they themselves have bactericidal properties. Solutions of chlorpromazine are incompatible with solutions of barbiturates and carbonates and with Ringer's solution (form precipitates). A 2.5% solution of chlorpromazine has a pH of 3.8–5.0.

Chlorpromazine is one of the most important neuroleptic substances.

One of the principal manifestations of the influence of chlorpromazine on the central nervous system is the sedative effect. The allaying of excitement which increases as the dosage of chlorpromazine is raised is accompanied by a reduction of motor activity and some relaxation of the skeletal muscles. When the proper doses are administered a condition develops which is close to normal sleep. The sedative action of chlorpromazine is observed in various pathological conditions marked by symptoms of excitement.

Chlorpromazine potentiates hypnotics, analgesics and local and general anesthetics. The action of antispasmodics is also heightened by chlorpromazine but in isolated cases chlorpromazine itself can cause convulsive manifestations. The drug is a potent antiemetic and allays hiccoughs.

A characteristic feature of chlorpromazine is its hypothermic action — the ability to lower the body temperature especially when the body is artificially cooled. It must, however, be noted that in isolated cases patients' temperature rises when the drug is administered parenterally; this is a consequence of its influence on the centres of thermoregulation and of its local irritating effect (Y. A. Popov and T. A. Nevzorova).

Chlorpromazine also has an adrenolytic effect: it reduces or even completely abolishes an elevation of the arterial pressure by adrenalin. The adrenolytic effect is not, however, universal: the hyperglycemic action of adrenalin is not reversed by aminazine. Chlorpromazine's blocking influence on the peripheral cholinergic systems and especially on the autonomic ganglia is weakly manifested.

Chlorpromazine depresses various interoreceptor reflexes; it reduces the permeability of the capillaries, has an antiphlogistic effect and is a weak antihistamine.

The arterial pressure (systolic and diastolic) falls under the influence of chlorpromazine and tachycardia often develops

The mode of action of chlorpromazine has not been studied sufficiently. The drug's diverse pharmacological effects are associated with its influence on the origin and transmission of the neural stimulus in various elements of the central and autonomic nervous systems. Another fact that must be taken into consideration is that chlorpromazine actively influences metabolism: it intensifies anabolic processes and creates a more «economical» condition of the body.

Chlorpromazine's influence on the reticular formation of the brain stem plays a definite role in its central action. According to contemporary findings, chlorpromazine blocks the reticular formation and abolishes its activating influence on the cerebral cortex. There are grounds for the view that the action of chlorpromazine is associated with its blocking influence on the adrenergic elements of the reticular formation (P. A. Anokhin).

Chlorpromazine has found wide application in medical practice.

In psychiatry, chlorpromazine's ability to reduce affective tension about psychomotor excitement and induce lengthy sedation of patients is particularly valuable. In psychiatric practice, chlorpromazine is used in schizophrenia (in the paranoid form, in catatonic and delirious states and in stupor), in manic excitement during the course of circular insanity, in the circular form of schizophrenia and other mental diseases, in the hypochondriac syndrome, in the depressive agitated state in patients with a senile psychosis, in prolonged alcoholic psychosis, in the «hang over» syndrome and seizures of delirium tremens in neuroses accompanied by insomnia and phobias, in vascular diseases (atherosclerosis and hypertensive disease) with psychic disorders.

In neurological practice, chlorpromazine is also prescribed in diseases accompanied by an elevation of the muscular tone (after apoplexy and the like). Chlorpromazine is sometimes used to overcome status epilepticus (when the usual methods of treatment are ineffective). For this purpose, the drug is administered intravenously or intramuscularly. It should be borne in mind that in epilepsy patients, chlorpromazine may cause attacks to become more frequent but ordinarily when it is used simultaneously with antispasmodics (phenobarbital or phenytoin), it intensifies their effect.

In children, chlorpromazine is also used in psychoses, in cases of excitement in the mentally retarded, in hallucinations, in impulsive seizures, in manic conditions, etc.

In surgery, chlorpromazine is used for the sedation of patients before operations, to potentiate analgesics and local and general anesthetics («potentiated anesthesia»), to prevent and treat shock and to prevent complications during the operation and the postoperative period (undesirable reflex reactions, vomiting, etc.). Chlorpromazine is used in artificial cooling of the body (hypothermia) in order to achieve a more rapid lowering of the body temperature and reduce side effects. Chlorpromazine is usually administered for this purpose in combination with other drugs (see Lytic mixtures below).

As an antiemetic, chlorpromazine is used in vomiting of pregnancy, and especially in oncological practice during ray therapy and treatment with chloroethylnamines. Chlorpromazine is extremely effective when administered in conjunction with analgesics in cases of persistent pain and in conjunction with barbiturates in persistent insomnia.

The drug is occasionally used in bronchial asthma. Favourable results have been reported in anorexia associated with various somatic and neurological diseases.

In the skin diseases clinic, chlorpromazine can be employed in pruritic dermatitis and other diseases.

Because of chlorpromazine's adrenolytic and hypotensive action, attempts have been made to use it in the treatment of hypertensive disease. However, the hypotensive effect is transitory and the use of the drug for this purpose requires a strict individualization of dosage and careful observation of the patient's condition, due to the possibility of a collaptoid reaction.

Chlorpromazine is administered orally intramuscularly or intravenously. When administered parenterally the effect is quicker and more intense. Orally the drug is given in tablets (or dragées) after meals. For intramuscular administration the necessary amount of ampouled 0.5% solution of chlorpromazine is diluted with 3–5 ml of 0.25–0.5% procaine hydrochloride solution or isotonic saline. The solution is injected deep into the muscle (upper outer quadrant of the gluteus maximus or the outer lateral surface of the thigh). For intravenous administration the necessary amount of chlorpromazine solution is diluted with 10–20 ml of 40% glucose solution or isotonic saline; it is infused slowly (in 5 min).

The dosage of chlorpromazine depends on the method of administration, the indications and the patient's age and condition. Orally adults are prescribed 0.025–0.05 or 0.1 g (25–50 or 100 mg) daily for the first 1–2 days of treatment (in 1–3 doses). When administered parenterally the dosage during the first 1–2 days should not exceed 0.05 g (50 mg) daily (1–2 administrations); subsequently the dosage may be increased, the daily dose ranging from 0.1 to 0.3 g (4–6 administrations of 0.025–0.05 g). To abort acute excitement the dose may be increased to 0.4 g and in rare cases somewhat higher. The maximal dosage for adults when administered orally or intramuscularly is 0.15 g for the single dose and 0.5 g for the daily dose. Maximal intravenous doses: single — 0.05 g daily — 0.2 g.

Children are prescribed from 0.025–0.1 g chlorpromazine daily depending on the age. It is mostly administered intramuscularly in 2 doses (before afternoon and night sleep).

In psychiatric practice treatment with chlorpromazine is usually lengthy (3–4 months or more) after treatment as an inpatient; treatment is usually continued on an outpatient basis with «maintenance» doses ($1/4$ – $1/3$ the dose given during the course of treatment).

Chlorpromazine can be applied alone or in combination with other medicines (bromides, hypnotics, reserpine, insulin, etc.).

In surgical practice so-called «lytic mixtures» are often employed. Besides chlorpromazine these mixtures contain antihistamines (diprazin, fenethazine, etc.), analgetics (promedol, etc.) and other substances (see Diethazine) which have an influence on the central and autonomic nervous systems. The composition of the lytic mixture and the content of the various ingredients may differ depending on the conditions. The following mixtures are examples of some in use: a) 2 ml 2.5% chlorpromazine, 2 ml 2.5% diprazin, 1 ml 2% promedol; b) 2 ml 2.5% chlorpromazine, 5 ml 0.5% fenethazine, 2 ml 2% promedol; c) 2 ml 2% chlorpromazine, 2 ml 2% medrol, 2 ml 2% promedol. The first mixture is used most often. The mixtures are administered intramuscularly or intravenously. A half dose is usually given an evening before the operation; the next day 1–2 hours before an operation a full dose is administered intramuscularly during the operation; half doses are administered intravenously should the necessity arise. When these mixtures are employed it is possible to make a substantial reduction in the amount of anesthetic used for the operation and to prevent or abate possible complications during the operation and the postoperative period.

Chlorpromazine may cause side effects associated with its local and resorptive action. If chlorpromazine solutions come in contact with the skin or mucosa they may cause irritation of the tissues. Intramuscular administration is often accompanied by painful infiltrates. Intravenous administration may cause injury to the endothelium. In order to avoid these complications chlorpromazine solutions are diluted with solutions of procaine hydrochloride or glucose. There may also be allergic reactions involving the skin and mucous membranes.

When chlorpromazine is taken orally dyspeptic symptoms are possible. Cases of hepatitis and leukopenia have been reported.

It should be borne in mind that the parenteral administration of chlorpromazine may cause an abrupt fall in the arterial pressure. In order to avoid

orthostatic collapse the patient should lie down for $1\frac{1}{2}$ —2 hours after the administration

When chlorpromazine is used for lengthy periods some patients develop what is known as a «neuroleptic syndrome», manifested in symptoms of parkinsonism indifference sluggish reaction to external stimuli and other psychic changes At times a prolonged subsequent depression is observed Stimulators of the central nervous system are used to abate the depression (see Piridrol and Meridil p 75)

Chlorpromazine is contraindicated in affections of the liver (cirrhosis hepatitis cythemolitic icterus etc) affections of the kidneys (nephritis acute pyelitis amyloid kidney lithiasis) impairment of the function of the hemopoietic organs progressive systemic diseases of the brain and spinal cord ulcer of the stomach and duodenum at a period of exacerbation decompensated heart disease pronounced hypotonia thromboembolism pronounced myocardiodystrophy, rheumocarditis and late stages of bronchoectasis Chlorpromazine (as well as promazine or mepazine) cannot be prescribed for individuals in a comatous state produced by barbiturates narcotics or alcohol

During treatment with chlorpromazine patients should be under careful observation by medical personnel The blood picture should be checked systematically In order to avoid the development of allergic dermatitis exposure of patients to the sun must strictly be prevented

When working with chlorpromazine (just as with other phenothiazine derivatives) precautionary measures must be strictly observed to prevent the possibility of powder or solutions coming in contact with the skin and mucous membranes

At the first appearance of symptoms of contact complications (itching of the skin or mucous membrane of the eyes edema of the skin of the lids back of the hand or forearm papular rash fall in the arterial pressure etc) the victim must at once be removed from contact with chlorpromazine and sent to a specialist (to a dermatologist if there are symptoms of skin complications)

Available in the form of tablets (dragées) of 0.025 g and in ampoules containing 5 ml 0.5% solution (for intramuscular administration) or 2 ml 2.5% solution (for intravenous administration) To be stored in hermetically sealed containers of amber glass or in sealed ampoules in a place protected from light observing safety precautions (List B)

Rp Chlorpromazini 0.025

D t d N 30 in tabul

S 1 tablet 3 times a day after meals

Rp Sol Chlorpromazini 0.5% 50

D t d N 6 in amp

S For intramuscular injections at 5 ml

first dilute with 5 ml 0.5% procaine hydrochloride solution

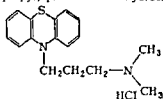
Rp Sol Chlorpromazini 2.5% 20

D t d N 6 in amp

S For intravenous infusions at 1—2 ml first dilute with 10—20 ml 40% glucose solution

PROMAZINE (Promazinum)

10 (2-D-methylaminopropyl) phenothiazine hydrochloride



Synonyms Centractil Protactyl Prozine Sediston Sparine Talofen Verophen

White crystalline powder freely soluble in water melting point 176—179.5°

Promazine differs from chlorpromazine in chemical structure only in the absence of a chlorine atom in position 2 of the phenothiazine nucleus. In its pharmacological properties promazine is also very similar to chlorpromazine. Like chlorpromazine it has a sedative effect, diminishes motor activity, potentiates and prolongs the effect of hypnotics and local and general anesthetics and has an antiemetic and hypothermic action. It is however inferior to chlorpromazine in its neuroplegic (sedative) action.

Experimental finding would show that promazine is approximately one half potent as chlorpromazine. In cases of psychic excitement the effect of chlorpromazine is manifested more distinctly.

In their peripheral cholino and adrenolytic action there is no essential difference between the two drugs. In chlorpromazine the antihistaminic effect is more pronounced. Promazine is somewhat less toxic than chlorpromazine, there is less local irritation and allergic reactions are observed less frequently.

In psychiatry indications for the use of promazine are the same as for chlorpromazine. It is especially used in cases with a mild course of the disease and in supportive therapy. Promazine may be employed in conjunction with chlorpromazine, alternating the two drugs particularly if there are infiltrates and allergic reactions from the use of chlorpromazine.

Promazine is administered orally, intramuscularly and intravenously. Orally it is given in tablets or dragees at 0.05 or 0.1 g (less frequently 0.15 g) per dose 2—4 times a day after meals. For supportive therapy it is prescribed in doses of 0.05, 0.1 or 0.15 g 1—2 times daily. Intramuscularly it is given in doses of 0.05, 0.1 or 0.15 g 2—3 times a day. The necessary amount of ampouled 2.5% promazine solution is diluted with 5 ml of 0.25—0.5% procaine hydrochloride solution or isotonic saline. Intravenously 1—2 ml 2.5% promazine solution is administered, the promazine being first diluted with 10—20 ml 40% glucose solution or isotonic saline. Methods for use, precautionary measures and duration of treatment are the same as for chlorpromazine.

In neurology, therapeutics, obstetrics, gynecology and dermatology promazine can be applied on an equal with chlorpromazine.

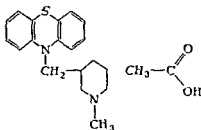
In surgery promazine can be employed as the basic ingredient of lytic mixtures in place of chlorpromazine and in the same amounts.

Promazine is tolerated better than chlorpromazine and side effects are less frequent. Nevertheless when using this drug and when working with it during production and packaging the same precautions should be observed as in the case of chlorpromazine.

Available in tablets (dragees) of 0.025 and 0.05 g and in ampoules containing 2 ml of the 2.5% solution.

To be stored in hermetically sealed containers of amber glass or in sealed ampoules in a place protected from light, observing safety precautions (List B).
MEPAZINE (Mepazinum)

10 (1-Methylpiperidyl 3-methyl) phenothiazine acetate



Synonyms Lacumin Pacalal Pecazine, Pecazinum

Fine white crystalline powder, freely soluble in water, melting point 69—70°. Solutions of mepazine like those of chlorpromazine are incompatible with solutions of barbiturates and carbonates

Mepazine differs from chlorpromazine in chemical structure in having an N-methylpiperidyl heterocyclic system in the side chain attached to the nitrogen atom of the phenothiazine nucleus. In its pharmacological properties mepazine is similar to chlorpromazine and promazine. It has a sedative, antiemetic and antispasmodic effect and potentiates hypnotics, analgesics and anesthetics. In its sedative effect however it is considerably less potent than promazine and chlorpromazine. In ordinary doses it does not cause drowsiness and its hypotensive action is less pronounced.

Mepazine also has an adrenolytic, cholinolytic and moderate antihistaminic effect. It is less toxic than chlorpromazine and there is usually no subsequent depression.

In psychiatry mepazine is mainly used in cases of neurosis and psychosis with symptoms of fright and emotional tension and in cases of exaggerated psychomotor activity. It has little effect in severe psychoses with agitation. More potent drugs such as chlorpromazine or promazine should likewise be used to abort extreme excitement.

Mepazine can be employed in conjunction with chlorpromazine.

In surgery mepazine is indicated in preparation for anesthesia and operative procedure as a sedative and to lessen the danger of shock intensifying the effect of analgesics and prevent postoperative complications. For controllable hypotension mepazine can be used in combination with ganglion blocking substances. Mepazine is also employed in autonomic dystonia and insomnia. It is given to potentiate hypnotics, prevent vomiting and relieve pain in childbirth.

Mepazine is administered orally, intramuscularly and intravenously. Orally it is given in tablets or dragees in doses of 0.025, 0.05 or 0.1 g, 1—3 times a day. For injections a 25% solution in ampoules is used. When administered intravenously the necessary amount is diluted with 10 ml 40% glucose solution. The infusion is made slowly. The single dose for parenteral administration is 0.025, 0.05 or 0.1 g, 1—3 injections are given daily.

Mepazine is usually tolerated well. In therapeutic doses it does not have a strong hypotensive effect and does not cause orthostatic collapse; it can therefore be used on a wider scale in the ambulant clinic than chlorpromazine. Treatment however should be carried out under close observation by medical personnel. The blood picture should be checked periodically. Because of mepazine's cholinolytic properties dryness in the mouth and constipation are possible.

Mepazine is contraindicated in diseases of the liver and kidneys.

Available in tablets or dragees of 0.025 and 0.05 g and in ampoules containing 1 ml of 25% solution.

To be stored in hermetically sealed containers of amber glass or in sealed ampoules in a place protected from light, observing safety precautions (List B).

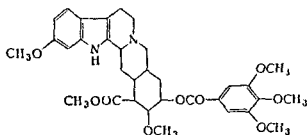
C Rauwolfia alkaloids

RAUWOLFIA (or *Rauwolfia serpentina* Benth.) is a perennial shrub of the Dogbane family (Apocynaceae) native to south and south east Asia — India, Ceylon, Java and the Malay Peninsula. First described in the XVI century by Leonhard Rauwolf, a German physician. Extracts of the roots and leaves have long been employed in Indian folk medicine. The plant, particularly the roots, contains a large number of alkaloids (reserpine, rescinnamine, reserpinine, ajmaline, ajmalicine, ajmalinine, rauwolfine, serpentine, serpagine, yohimbine etc.).

The Rauwolfia alkaloids have interesting pharmacological properties. Some of them, especially reserpine and to a less degree, rescinnamine, have a characteristic sedative and hypotensive effect, while others (ajmalicine, rauwolfine, serpagine and yohimbine) have an adrenolytic effect. Reserpine and some of the other alkaloids listed are found not only in *Rauwolfia serpentina* but also in *R. canescens* Linn, *R. micrantha* Hook, *R. tetraphylla* L., *R. heterophylla* Roem et Schult, as well as in other species of this genus.

Reserpine is at present widely used in medical practice. The alkaloids deserpidine and rescinnamine are also applied abroad. Moreover, a number of preparations are available which contain the total alkaloids of *Rauwolfia*: Gen-don, Guiline, Raudixin, Raupina, Rauwicon, Rauwifoid, Rauwiston, Rauwoldin, Rivadescin, Wolfina, etc.

RESERPINE (Reserpinum)



Reserpine is the principal alkaloid of *Rauwolfia*. It is an ester which on hydrolysis yields reserpinic acid, methanol and 3, 4, 5 trimethoxybenzoic acid. Reserpinic acid can be considered a derivative of indole.

The synthesis of reserpine was accomplished in 1956 by Woodward.

Reserpine is sold abroad under various names: Banasil, Crystoserpin, Escaserp, Quiescin, Raunorin, Rau Sed, Rausedyl, Resercen, Reserpoid, Residin, Roxinoid, Sandril, Sedaraupin, Serlin, Serollia, Serpanray, Serpasil, Serpate, Serpen, Serpicon, Serpiloid, Serpin, Tenserpin, etc.

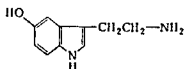
White crystalline substance, freely soluble in glacial acetic acid and in organic solvents, very sparingly soluble in water. Melting point 261–263°.

Reserpine's principal pharmacological properties are its sedative influence on the central nervous system and its hypotensive effect. It deepens and intensifies physiological sleep, potentiates barbiturates and other hypnotics and inhibits interoreceptor reflexes. The hypotensive action is manifested very strongly but the effect develops gradually. Unlike chlorpromazine, reserpine has no adrenolytic action. It produces a number of parasympathomimetic effects: retarding of cardiac activity (with lengthening of diastole), intensification of gastrointestinal peristalsis, increase in the formation of hydrochloric acid in the stomach, miosis. Reserpine has no ganglion blocking action. It causes hypothermia, and lowers metabolism to some extent.

The mode of action of reserpine is not sufficiently clear, but there are grounds for considering that it acts selectively on the subcortical centres raising the tone of the parasympathomimetic (cholinoreactive) elements. It is possible that to a certain extent the action of reserpine is associated with its influence on the metabolism of 5 hydroxytryptamine (serotonin) and pyrocatecholamines (noradrenalin and adrenalin). It has been established that the introduction of reserpine into the body causes a substantial reduction in the content of these biogenic amines in the central nervous system and in other organs and tissues; the excretion in the urine of decomposition products of serotonin (5 hydroxyindolacetic acid, etc.) increases. Information is now available on the role of noradrenalin and serotonin in the function of the central nervous

system. One of the things indicating that the action of reserpine depends on influence on the activity of these amines is the ability of inhibitors of monoamine oxidase (see Iprazid p. 76), which retard the decomposition of serotonin, noradrenalin to counteract the sedative effect of reserpine.

The similarity in the chemical structure of reserpine and serotonin speaks in favour of a connection between the action of the two compounds. They are derivatives of indole.



Serotonin (5-hydroxytryptamine)

Reserpine is chiefly used in the treatment of hypertensive disease and mental diseases. Under the drug's influence there is a gradual lowering of maximal and minimal arterial pressure in various forms of hypertensive disease (including hyperfunction of the thyroid gland), the best effect is observed in early stages of the disease in the absence of organic changes in the cardiovascular system. A therapeutic effect usually appears in 2–6 days after the beginning of treatment. The hypotensive effect remains for a relatively long time after the administration of reserpine is discontinued.

Reserpine is usually administered orally in the form of tablets. Sometimes intramuscular or intravenous administration is resorted to, but parenteral administration has no significant advantages over the oral method.

The dosage of reserpine and the duration of treatment must be individualized.

In hypertensive disease administration of reserpine is begun with a dose of 0.1–0.3 mg (0.0001–0.0003 g) daily; the drug is taken after meals. In some cases it is enough to continue these doses, but in others the dose is gradually raised to 0.5–1 mg daily; if there is no effect the dose can be increased to 1.5–2 mg daily. If there is no hypotensive effect in 10–14 days the drug is withdrawn. If an effect does ensue the dose is gradually lowered to 0.5 and 0.1 mg daily. Treatment with small or "maintenance" doses is continued for a lengthy period (several months) under a physician's observation.

When necessary reserpine can be prescribed in combination with other hypotensive agents, particularly a pressor as well as hexonium, azomethonium bromide and other ganglion blocking drugs (see p. 107).

Reserpine is also employed in light forms of cardiac insufficiency with tachycardia (along with heart glycosides), in hypersympathicotonia, thyrotoxicosis (along with thyrostatic substances) and in late toxicosis of pregnancy.

In psychiatry reserpine is applied in neuro-psychic disorders having elevated arterial pressure as a basis, in psychomotor excitement in schizophrenic patients, in manic excitement in the course of circular psychosis and the circular form of schizophrenia and other mental diseases, in depressive agitated condition in patients with a senile psychosis, in persistent insomnia and other diseases.

The drug is usually prescribed orally at an initial dosage of 0.25 mg daily; this is gradually raised to 0.5, 1 and 5 mg daily and if necessary to 10 mg daily (in 2–4 administrations). When administered intramuscularly a 0.1% solution of reserpine is used; this is supplied in ampoules of 1 ml containing 0.001 g (1 mg) in a special solvent. Treatment is begun with the administration of 0.5 ml twice a day, gradually increasing the dose to 1–2 ml 2–3 times

day Large doses are ordinarily used for excited patients especially in schizophrasia

In cases of neurosis reserpine is prescribed in small doses beginning at 0.25 mg 2-3 times a day and increasing the dosage to 0.5 mg 3-4 times a day

In mental diseases the course of reserpine treatment is from 1½ to 4 months or more After the course of inpatient treatment patients are prescribed «maintenance» doses of 0.5-1 mg 1-3 times a day

Maximal doses of reserpine for adults single—0.001 g (1 mg) daily—0.005 g (5 mg) When the drug is prescribed in large doses there should be a special note in the prescription

Children are prescribed reserpine in the following dosages up to 1 year old—maximum of 0.1 mg 1-2 times daily up to 5 years old—0.1 mg twice daily from 6 to 12 years—0.1 mg 2-3 times daily

When given in small doses reserpine as a rule causes no side effects When given in large doses and in cases of heightened sensitivity there may be hyperemia of the mucosa of the eyes, skin rash pain in the stomach diarrhea bradycardia weakness vertigo dyspnea nausea, vomiting and nightmares When used for lengthy periods symptoms of parkinsonism are possible During course treatment in patients with mental diseases a feeling of anxiety and unrest persistent insomnia and a state of depression may develop

If there are side effects the dose of reserpine should be lowered or the drug should temporarily be withdrawn In case of pain in the stomach and diarrhea cholinolytic agents are prescribed in case of parkinsonism atropine tropacine amizyl or similar drugs are given In cases of pronounced depression stimulants of the central nervous system are used (see Piridol and Meridol p 75) When prescribing the drug on an outpatient basis the possibility of the development of somnolence and general weakness must be borne in mind

Reserpine is contraindicated in severe organic cardiovascular diseases with symptoms of decompensation and marked bradycardia in coronary sclerosis cerebral sclerosis and nephrosclerosis and in ulcer of the stomach and duodenum

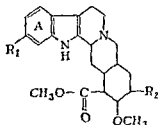
Available in powder form and in tablets of 0.0001 g (0.1 mg) and 0.00025 g (0.25 mg)

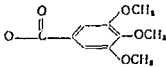
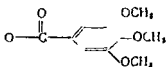
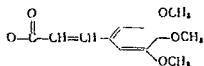
Reserpine in powder form is to be kept locked (List A) safety precautions are to be observed in storing tablets (List B) To be stored in tightly closed containers in a dry place protected from light

Rp Reserpini 0.0001
D t d N 20 in tabul
S 1 tablet twice a day after meals

DESERPIDINE RESCINNAMINE AND OTHER RAUWOLFIA DRUGS

Deserpidine is obtained from the plant *Rauwolfia canescens* In its chemical structure it differs from reserpine in not having a methoxy group in position 11 of ring A of the reserpine molecule i.e. it is 11-desmethoxyreserpine



Name of alkaloid	R ₁	R ₂
Reserpine	OCH ₃	
Deserpidine	—	
Rescinnamine	OCH ₃	

Rescinnamine which is obtained from *Rauwolfia serpentina* differs from reserpine in having in the side chain the residue of trimethoxycinnamic acid instead of the residue of trimethoxybenzoic acid

Deserpidine is also known as Recanescin Raunormin and Harmony1 while rescinnamine is likewise sold under the name of Moderil

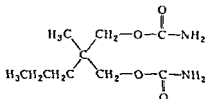
Both alkaloids have a sedative and hypotensive effect but are less potent than reserpine they are used abroad as reserpine like substances

The action of the total alkaloid preparations of *Rauwolfia* (Gendon Raupina Rauwiloid etc) depends for the most part on their reserpine content They are prescribed in large doses since they contain only small amounts of reserpine They are taken in a dosage of 2 mg 1—3 times a day after meals The effect from these preparations is somewhat less marked and for that reason they have not found wide application in psychiatry

D Derivatives of propanediol and diphenylmethane

MEPROTAN (Meprotranum)

2 Methyl 2 n propyl 1 3 propanedioldicarbamate



Synonyms Amepromat Anathymon Andaxin Aneurul Ansiatan Ansil Artolon Bobamat Cirpon Diveron Equanil Erina Gadexyl Mepavlon Meproban Meprobamate Meprospan Milltown Nephentine Oásil Pankalma Paxin

Perequil, Pertranquile Probamato, Procalmadiol, Quaname, Quanil, Restenil, Restinal, Sedanyl, Sedazil, Setran, Tensonal, Tranquil, Tranquiline Tranquisan, Trelmar, Urbil

White crystalline powder of bitter taste, freely soluble in ethyl alcohol and acetone, soluble in warm water. Melting point 105—106°

Meprotran has a sedative influence on the central nervous system it potentiates hypnotics and has pronounced antispasmodic activity. It somewhat lowers the body temperature and in relatively large doses relaxes the skeletal muscles.

The mechanism by which meprotran relaxes the muscles is essentially different from that of curarelike drugs. It exerts no influence on the transmission of impulses through the neural muscular synapses but blocks the intercalated neurons of the spinal cord, thalamus, and hypothalamus. Because of this peculiarity of its action it has been suggested that meprotran and similarly acting drugs should be called "central relaxants" (Berger). The first member of this group to be used as a drug was 3 (o toloxy) 1,2 propanediol or myanesin (synonyms Mephensesin, Daserol, Myoxane, Tolserol, etc.). Because of its transitory action, low effectiveness when taken orally and relatively high toxicity, myanesin has practically lost significance as a drug. Meprotran is considerably more potent; it is effective when administered orally and is only slightly toxic.

Unlike the neuroplegic substances of the chlorpromazine and reserpine group, meprotran has no influence on the autonomic division of the nervous system and does not act directly on the cardiovascular system, the respiration or the smooth musculature.

Meprotran is mostly used in the treatment of nervous and mental diseases. The drug's sedative effect is most pronounced in conditions of anxiety, fright, internal tension and exaggerated excitability in cases of neurosis and psychopathy, as well as in disturbed sleep. A marked improvement is observed in cyclothymia without deep depression, and in mild involutional melancholy. The best effect is seen in patients with mild depression; meprotran has little effect in pronounced depressive conditions, agitation and delirium.

Meprotran can be used in combination with chlorpromazine during the basic course of treatment and for supportive (ambulant) therapy after the course of inpatient treatment. Meprotran can also be used in combination with other sedatives (amizyl, etc.).

It has been reported that meprotran is effective in the treatment of mild forms of epilepsy in diseases of the nervous system accompanied by elevated muscular tone and in diseases of the joints accompanied by muscular spasms.

As a sedative, meprotran can have a beneficial effect in autonomic dystonia, the initial forms of hypertensive disease, ulcer of the stomach, dermal pruritus, etc. In cases of insomnia, meprotran can be used alone or in combination with hypnotics.

In surgery meprotran can be used in preparing patients for operations by allaying nervous excitement, diminishing the feeling of fear and lowering muscular tenseness to some degree.

Meprotran is administered orally in tablets in a dosage of 0.2—0.4 g 3—4 times daily. If necessary the daily dose can be increased to 2—3 g. Children are prescribed smaller doses: from 5 to 8 years old — 0.1 g 3—4 times a day, from 8 to 14 — 0.2 g 3—4 times a day. The course of treatment averages 1—2 months. When discontinuing treatment the dose should be reduced gradually.

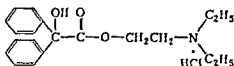
Meprotran is usually tolerated well. In isolated cases there may be allergic symptoms (rash, etc.), dyspeptic symptoms, drowsiness, a feeling of heaviness in the extremities and impairment of coordination of movements. These manifestations usually pass away in 1—2 days after the drug is withdrawn.

In isolated cases euphoria is observed. There are reports in the literature of the possibility of tolerance to the drug being developed. Treatment with meprotran should be carried out under the observation of a physician.

Available in tablets of 0.2 and 0.4 g To be stored in a cool dry place observing safety precautions (List B)

AMIZYL (Amizylum)

Diethylaminoethyl benzylate hydrochloride



Synonyms Aclozine, Amitakon, Arcadin, Benactina, Benactizine, Cafron, Cevanol, Lucidil, Nervatil, Neuractil, Neurobenzile, Nutinal, Parasan, Parpon, Phobex, Procalm, Stoikon, Suavitil, Tranquilline, Valladan

White crystalline powder, freely soluble in water. Melting point 175—176°. Solutions undergo hydrolysis on long standing.

In chemical structure and pharmacological properties amizyl is very similar to the esters of diphenylacetic acid (Spasmolytin and the like, p 104) and especially to Benzacin (p 105), which is a dimethyl homologue.

Amizyl has diverse pharmacological properties. It has a moderate spasmolytic, antihistaminic, antiserotonergic and local anesthetic effect, but its cholinolytic properties are the most pronounced; it blocks the peripheral and central cholinolytic systems. Under the influence of amizyl the excitatory effects of the vagus are abolished, the pupils are dilated, the secretion of the glands is reduced and the activity of the smooth muscles inhibited and their tone lowered. The influence on the central nervous system is manifested in a depression of the spasmodic effect of anticholinesterase and cholinomimetic substances (physostigmine, galanthamine, arecoline, etc.) and the prevention and overcoming of changes in the electroencephalogram caused by them, as well as in a sedative effect and potentiation of barbiturates and other hypnotics, analgesics and local anesthetics.

The drug abolishes symptoms of experimental neurosis in animals, and suppresses the cough reflex to a marked degree.

As a substance having a central cholinolytic and sedative action amizyl finds application in the treatment of some nervous and mental diseases for the most part in asthenic and neurotic conditions accompanied by unrest, anxiety, strain, fear and mild depression.

Amizyl normalizes autonomic reactions and improves sleep and patients' general condition.

Amizyl is not used in severe states of depression or excitement. It can be employed in conjunction with chlorpromazine, reserpine, meprobamate and barbiturates. As a central cholinolytic agent amizyl can prevent or abate manifestations of parkinsonism caused by phenothiazine derivatives and reserpine. When used simultaneously with reserpine, the cholinomimetic effects from the latter are diminished.

Like other cholinolytic agents amizyl is also effective in diseases accompanied by spasms of the smooth muscles of the internal organs.

Amizyl is very convenient as a mydriatic for diagnostic purposes since it induces a pronounced but transitory dilation of the pupil.

Amizyl can be prescribed for patients suffering from cough and can likewise be administered to suppress the cough reflex during operations.

For the treatment of nervous and mental diseases amizyl is prescribed orally in tablets 0.001—0.002 g (1—2 mg), 3—5 times a day. The course of treatment is for 4—6 weeks. As an antispasmodic and anticough agent it is administered orally in a dose of 0.001—0.002 g. In order to dilate the pupil 1—2 drops of 1% aqueous solution are instilled into the conjunctival sac because of the hydrolysis that takes place on long standing fresh solutions are recommended.

The complications that may occur after taking amizyl are mostly due to its cholinolytic action. Like atropine it may cause dryness in the mouth, acceleration of the pulse and dilation of the pupils. Because of amizyl's local anesthetic properties a numbness of the tongue and palate may ensue when it is taken orally. At times there is slight vertigo. The drug is contraindicated in glaucoma.

Available in powder form and in tablets of 0.001–0.002 g (1–2 mg). To be kept locked (List A) in a cool dry place in hermetically closed containers.

E Miscellaneous sedatives

MAGNESIUM SULPHATE (*Magnesium sulfuricum*)

Magnesium sulphate heptahydrate Epsom salts bitter salts (*Sal amarum*) $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$

Colourless prismatic crystals which effloresce in warm dry air, freely soluble in water (1 in 1 in cold and 3.3 in boiling water), very sparingly soluble in alcohol. Aqueous solutions have a bitter salt taste.

Solutions for injections are sterilized in running steam at 100° for 30 min or in an autoclave at 120° for 15–20 min.

When administered parenterally magnesium sulphate has a sedative effect on the central nervous system, weakening the excitatory process; a sedative, hypnotic or anesthetic effect may be observed depending on the dose. When administered orally the influence on the central nervous system is manifested to a less degree because of poor absorption, and the drug acts mainly as a laxative. This is due to changes in the osmotic pressure, absorption of water from the gut is retarded, the intestinal contents are thinned and the interoreceptors irritated which facilitates the act of defecation.

Magnesium sulphate also has a bile expelling action; this is associated with the reflexes arising from irritation of the nerve endings in the mucous membrane of the duodenum.

Another characteristic property of magnesium sulphate is its depressing influence on neuromuscular transmission. When administered parenterally it may have a curarelike effect, especially in large doses.

The drug lowers the excitability of the respiratory centre; administered parenterally, large doses may easily cause respiratory paralysis. The arterial pressure is lowered somewhat as a consequence of the drug's general sedative action, an effect that is more pronounced in patients with hypertensive disease.

Magnesium sulphate is excreted by the kidneys and diuresis is observed during the process.

Calcium ions are antagonists of magnesium ions. A reduction in the calcium content of the blood is accompanied by an intensification of the action of magnesium sulphate. Calcium salts are used as antidotes in cases of poisoning with magnesium sulphate.

Magnesium sulphate is mostly used as a sedative, anticonvulsive, spasmolytic, laxative or bile expelling agent. It is not employed alone as an anesthetic due to the small range of its anesthetic action — anesthetic doses may easily cause paralysis of the respiratory centre; it is used however to potentiate other anesthetics and analgesics.

When treating hypotensive disease (for the most part in early stages) 5, 10 or 20 ml of 25% magnesium sulphate solution is injected intramuscularly. The course of treatment consists of 15–20 daily injections. Along with a lowering of the arterial pressure, an abatement of symptoms of stenocardia may be observed. It has been reported that the regular administration of small doses orally (1–2 g to half a glass of water on an empty stomach) also promotes an improvement in patients' condition and retards the development of atherosclerosis.

When using magnesium sulphate to allay pain during labour, 5, 10 or 20 ml of a 25% solution is injected intramuscularly, sometimes in combination with

analgetics In nephropathy of pregnancy the drug is injected intramuscularly in the same concentration 20 ml 4 times daily When prescribing magnesium sulphate for pregnant patients the possibility of a depression of the contractile ability of the uterine muscles must be borne in mind — this may necessitate the use of labour stimulating drugs

In convulsions 5 10 or 20 ml of 25% solution is administered intramuscularly

As a laxative adults are prescribed 10—30 g orally in half a glass of water the dosage for children is 1 g per year of the patient's age In cases of chronic constipation enemas can be used (100 ml of 20—30% solution) As a bile expelling agent 1 tablespoonful of 20—25% solution is given orally 3 times a day the administration of a warm solution through a duodenal sound is also practised (50 ml of 25% solution or 100 ml of 10% solution)

In lead colic and retention of the urine magnesium sulphate is employed as a spasmolytic 5—10 ml of a 10—20% solution is administered intramuscularly or 5—10 ml of a 5% solution intravenously or the drug can be given in the form of an enema

Magnesium sulphate is likewise used in various forms of poisoning In cases of poisoning with soluble barium salts stomach lavage is performed with a 1% solution or 20—25 g in a glass of water is given orally (in order to form non-poisonous barium sulphate) In chronic poisoning with mercury, arsenic or tetraethyl lead 5—10 ml of 5—10% solution is administered intravenously

Parenterally magnesium sulphate must be administered with caution bearing in mind the possibility of respiratory depression Solutions must be infused into the veins slowly If respiration should be depressed calcium chloride is administered intravenously (5—10 ml of 10% solution) oxygen or carbogen is given and artificial respiration is begun

Available in powder form and in ampoules containing 25 10 or 20 ml of 25% solution

Magnesium sulphate in powder form is to be stored in tightly closed containers

Rp Sol Magnesi sulfurici 25% 100

D t d N 3 in amp

S 5—10 ml intramuscularly

Rp Magnesi sulfurici 300

DS One dose to be dissolved in half a glass of warm water (laxative)

VALERIAN — rhizome and root (*Rhizoma et radix Valerianae*)

Cleaned washed and dried rhizomes and roots of cultivated and wild medicinal valerian (*Valeriana officinalis* L.) of the Valerian family (*Valerianaceae*) found almost everywhere in the USSR Contains an essential oil the principal constituent of which is the ester of borneol and isovaleric acid also contains free borneol and isovaleric acid other organic acids (including valerenic acid $C_{15}H_{22}O$ which has a strong spasmolytic effect) alkaloids (valerine and choline) tannin sugars and other substances

Valerian preparations reduce the excitability of the central nervous system and also have spasmolytic properties They are used as sedatives in nervous excitement insomnia cardiovascular neurosis gastrointestinal spasms etc often in combination with other sedatives and cardiants

Valerian Infusion (*Infusum Valerianae*) Prescribed for adults in doses of 1 tablespoonful (5—10 g or more of root to 200 ml of water 3—4 times a day) older children are given 1 dessert spoonful and younger children 1 teaspoonful (2 g of root per 100 ml water)

Valerian tincture (*Tinctura Valerianae*) (20% tincture prepared with 70% alcohol)

Transparent liquid of reddish brown colour with characteristic aromatic odour and sweetish bitter spicy taste Darkens under the influence of sunlight

Adults are given 20—30 drops 3—4 times a day, children are given doses of 1 drop for each year of their age

Ethereal valerian tincture (*Tinctura Valerianae aetherea*)

Prepared from 100 g valerian rhizomes and roots, 500 ml alcohol and 300 ml ether. Transparent, yellowish brown liquid with acid reaction, and characteristic aromatic odour, taste at first pungent and then sweetish bitter spicy. Darkens under the influence of sunlight.

Adults are prescribed 20—30 drops 3—4 times a day, children are given doses of 1 drop for each year of their age.

Thick valerian extract (*Extractum Valerianae spissum*)

Thick extract of dark brown colour, characteristic valerian odour and bitter spicy taste.

Usually administered in the form of pills, in doses of 0.04—0.05 g.

MOTHERWORT—herb (*Herba Leonuri*)

Stems with flowers and leaves gathered at time of flowering and dried. The species used are the five leaved motherwort (*Leonurus quinquelobatus* Gelib L. villosus Desf.) and common motherwort (*Leonurus cardica* L.) of the mint family (Labiatae). Contains volatile oil, saponins, tannins and alkaloids.

Administered in the form of an infusion or tincture as a sedative in exaggerated nervous excitability, cardiovascular neurosis and early stages of hypertensive disease. In the character of their action motherwort preparations are similar to those of valerian. Sometimes prescribed in the form of a mixture, the other ingredients being valerian root and caraway and fennel seed.

Motherwort tincture (*Tinctura Leonuri* 20% tincture prepared with 70% alcohol)

Transparent liquid of greenish brown colour, bitter taste and faint aromatic odour.

INCARNATE PASSION FLOWER (*Passiflora incarnata*)

Flowering liana which grows wild in South America and is cultivated in the USSR. Passion flower infusions and extracts have a sedative action on the central nervous system and possess antispasmodic properties.

A fluid alcohol extract is used (prepared with 70% alcohol) dark brown liquid with a greenish tint, bitter taste. Prescribed in cases of heightened excitability, insomnia, etc., in doses of 15—40 drops 3 times a day. Course of treatment 30—40 days. Contraindications: stenocardia, myocardial infarction and atherosclerosis of cerebral and coronary vessels.

Rp Extr *Passiflorae incarnatae* fluidi 15.0

DS 20 drops 3 times a day

COMMON HOPS (*Humulus lupulus* L.)

In folk medicine use is made of an infusion of the strobiles and glandular trichomes of the hop (*Glanduli Lupuli*), a plant of the mulberry family (Moraceae), gathered in August and September. Contains a bitter substance, lupulin which has a sedative effect. Used as an analgetic in cystitis and in urinary urgency, and also as a sedative for the nervous system.

III. ANALGETICS, FEBRIFUGES AND ANTIPHLOGISTICS

A Analgetics of the opium group and their synthetic substitutes

OPIUM (*Laudanum Meconium*)

Air dried milky juice from incisions on unripe capsules of different varieties of the opium poppy — *Papaver somniferum* L. — of the family Papaveraceae. Lumps of various size or soft amorphous mass of dark brown colour with characteristic odour and bitter taste. Partially soluble in water with the formation of a brown solution having an acid reaction.

Contains morphine, papaverine, codeine, thebaine, narcotine and other alkaloids. The morphine content in opium comes to 10—11%. The narcotine content

ranges between 8 and 10%, codeine — 1.5—3%. The other alkaloids are contained in smaller amounts

In medical practice powdered opium and galenic preparations obtained from it (extracts and tinctures) are used, as well as individual alkaloids (morphine, codeine and others)

Opium preparations have a characteristic influence on the central nervous system. They diminish the reception of pain sensations and induce euphoria, in large doses they have a hypnotic effect, they lower the excitability of the respiratory and cough centres, and have an inhibitory influence on the motor function of the stomach and intestine. The action of opium and galenic preparations obtained from it coincide to a large degree with the action of morphine.

Opium and opium preparations are used as analgetics in pain from various causes (trauma postoperative pain, inflammatory processes in the internal organs — peritonitis, pleuritis, cholecystitis, intestinal and kidney colics, etc.), they are used in insomnia resulting from severe pain and in persistent coughing associated with exaggerated excitability of the motor centre, as well as in diarrhoea of nontoxic and nondysenteric origin, etc.

Children up to 5 years old are not prescribed opium because of the high sensitivity of their respiratory centre to the drug and the possibility of respiration being depressed.

Older children are prescribed opium only in cases of extreme necessity.

Other contraindications to the use of opium preparations and alkaloids are senility, insufficiency of the respiratory centre and extreme general emaciation.

The lengthy use of opium preparations may cause the development of tolerance and habituation.

The following opium preparations are used:

Powdered opium (*Pulvis Opii*, *Opium pulveratum* or *Opium purum*) Powder of light yellow to light brown colour and characteristic odour. Contains about 11% morphine. Administered orally in powders and tablets, also administered in the form of suppositories. Doses for adults 0.01—0.03 g.

Maximal doses for adults single — 0.1 g, daily — 0.3 g.

Maximal doses for children 5—6 years old, single — 0.01 g; daily — 0.03 g. From 7 to 9 single — 0.015 g, daily — 0.015 g. From 10 to 14 single — 0.015—0.02 g, daily — 0.045—0.06 g.

Dry extract of opium (*Extractum Opii siccum*) Aqueous extract of opium. Brown powder forming turbid, extremely bitter solution with water. Contains about 20% morphine.

Prescribed in powders, pills and suppositories, doses for adults 0.01—0.02 g. Suppositories ready for use, containing 0.01 g opium extract are available.

Maximal doses for adults single — 0.05 g, daily — 0.15 g.

Maximal doses for children 5—6 years old single — 0.005 g, daily — 0.015 g. From 7 to 9 single — 0.0075 g, daily — 0.025 g. From 10 to 14 single — 0.01 g, daily — 0.03 g.

Simple tincture of opium (*Tinctura Opii simplex*)

Water alcohol tincture of opium, contains about 1% morphine. Transparent reddish brown liquid with characteristic taste and odour of opium. 1 ml corresponds to 43 drops.

Adults are prescribed doses of 5—10 drops.

Maximal doses for adults single — 0.5 ml (22 drops), daily — 1.25 ml (55 drops).

Maximal doses for children 5—6 years old single — 3 drops, daily — 6 drops, from 7 to 9 single — 4 drops, daily — 8 drops, from 10 to 14 single — 5—7 drops, daily — 10—15 drops.

Children are given the tincture a maximum of 2 times a day. If somnolence should develop the preparation is withdrawn.

Opium opium tablets opium extract and simple tincture of opium are kept locked (List A)

Opium is an ingredient of the following combined preparations (available ready for use)

Benzoated tincture of opium (Tinctura Opi benzoica)

Formula simple tincture of opium—50 ml benzoic acid—20 g camphor—10 g anise oil—5 g, 70° alcohol—make up to 1 l Contains 0.045–0.055% morphine

Transparent brownish yellow liquid camphor anise odour sweetish spicy taste acid reaction

Used as an expectorant and soothing cough remedy both alone and in combination with other drugs Doses for adults—20–40 drops doses for children—1 drop per year of age

Standard tablets are available under the name «Paregoric» which can be used in place of benzoated tincture of opium

Paregoric Composition powdered opium—0.0045 g powdered camphor—0.01 g benzoic acid—0.04 g anise oil—0.005 g lactose—0.32 g

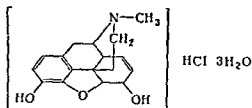
One tablet is taken 2–3 times a day

Pectol Tablets containing the following dry extract of thermopsis—0.01 g opium (powdered)—0.01 g, sodium bicarbonate—0.2 g licorice powder with anise oil—0.2 g

Used as an expectorant and soothing cough remedy 1 tablet 2–3 times a day

MORPHINE (Morphinum)

The principal alkaloid of opium the hydrochloride is used (Morphinum hydrochloricum Morphini hydrochloridum)



White silky needles or white crystalline powder turns slightly yellow on standing Soluble in water (1:25 in cold and 1:1 in boiling water) sparingly soluble in alcohol (1:50) sparingly soluble in chloroform and ether Insoluble with alkalis Solutions are sterilized in running steam at 100° for 30 min For stabilization 1 ml 0.1 N HCl is added to each 100 ml of 1% solution The solution has a pH of 3.0–3.5

Morphine is the principal member of the group of analgesics, i.e. agents that cause a lowering of sensitivity to pain, without loss of consciousness or essential changes in other forms of sensibility It has a mild hypnotic effect which is more pronounced in insomnia caused by pain The analgesic effect is accompanied by the development of euphoria—it is this that may give rise to addiction and chronic poisoning (morphinism)

According to present conceptions the analgetic effect of morphine is associated with its depressing influence on the thalamic regions and the hindering of the transmission of pain impulses to the cerebral cortex

Morphine has an inhibitory influence on conditioned reflexes lowers the summation ability of the central nervous system (V. V. Zakusov) and potentiates hypnotics and local and general anesthetics It lowers the excitability of the respiratory and cough centres Small doses cause a retarding of breathing with an increase in amplitude large doses cause a further retarding of breathing and a diminution in depth with a lowering of pulmonary ventilation Toxic doses

cause periodic breathing of the Cheyne Stokes type with subsequent stoppage of respiration. The depression of respiration caused by morphine is abolished by atorphine (see p 50).

Morphine excites the centre of the vagus nerves, which may lead to bradycardia. It also excites the vomiting centre.

Morphine inhibits the motor and secretory activity of the gastrointestinal tract. It raises the tone of the sphincters of the bladder and stimulates the contractions of the bile ducts and the uterus, it raises the tone of the bronchial muscles.

Basic metabolism is lowered by morphine, and the body temperature falls.

Morphine is quickly absorbed when taken orally or administered subcutaneously. Its action develops within 10—15 min after subcutaneous injections and in 20—30 min after administration by mouth. The effect of the single dose lasts 3—5 hours.

Morphine is used as an analgesic in trauma and in various diseases accompanied by severe pain (malignant neoplasms, myocardial infarction etc.), it is also used in preparing patients for an operation and in the postoperative period in cases of insomnia caused by severe pain, at times in severe coughing and in severe dyspnea associated with acute cardiac insufficiency. Morphine is also used sometimes in allaying pain during childbirth, but it must be borne in mind that the drug passes through the placental barrier.

Morphine is prescribed subcutaneously (usually 1 ml of 1% solution for adults) orally (0.01—0.02 g in powders or drops) and sometimes in the form of suppositories (0.01 g).

In order to avoid side effects associated with the excitation of the vagus (particularly bradycardia) and the elevation of the tone of the sphincters atropine is often administered simultaneously with morphine.

Maximal doses for adults (orally and subcutaneously) single — 0.02 g daily — 0.06 g.

Maximal doses for children: 2 years old single — 0.001 g daily — 0.002 g from 3 to 4 years single — 0.0015 g daily — 0.003 g from 5 to 6 years single — 0.0025 g daily — 0.0075 g from 7—9 years single — 0.003 g daily — 0.01 g from 10 to 14 single — 0.003—0.005 g, daily — 0.01—0.015 g. Infants up to 2 years old are not prescribed morphine.

Contraindications: the same as for opium.

Available in powder form and in ampoules containing 1 ml of 1% solution. To be kept locked (List A) in tightly closed bottles of amber glass in a place protected from light.

OMNOPON (Omnoponum)

A mixture of the hydrochlorides of the alkaloids of opium containing the equivalent of 48—50% morphine base and from 29.9 to 34.2% of the bases of the other alkaloids.

Brownish yellow or brownish pink powder soluble in water (1:15) and in alcohol (1:50).

A similar preparation is sold abroad under the names Domopon, Opialum, Pantopon, Papaveralum and Sompon.

1 ml of 1% omnopon solution (and proportionally 1 ml of 2% solution) contains the following alkaloids: morphine hydrochloride — 67 mg (134 mg), narcoline — 27 mg (54 mg), papaverine hydrochloride — 0.36 mg (0.72 mg), codeine — 0.72 mg (1.44 mg), thebaine — 0.05 mg (0.1 mg). pH of 1% and 2% solutions 2.8—3.2.

Omnopon is prescribed orally, subcutaneously and rectally in suppositories, the indications being the same as for morphine. Omnopon is often tolerated better than morphine; spasms of the smooth muscles are less frequent. Omnopon is prescribed for adults in doses of 0.01—0.02 g. Children can be prescribed 1% solution orally in the following dosages: from 2 to 5 years old — 2—6 drops, 6—10 years old — 8—12 drops. Subcutaneously adults are given 1 ml of 1% or

2% solution Children from 2 to 5 years old are given injections of 0.1–0.2 ml of 1% solution from 6 to 10 years old — 0.3–0.4 ml

Maximal doses for adults (orally and subcutaneously) single — 0.03 g daily — 0.1 g

Maximal doses for children 2 years old single — 0.002 g daily — 0.004 g from 3 to 4 years old single — 0.003 g daily — 0.006 g from 5 to 6 single — 0.005 g daily — 0.015 g from 7 to 9 single — 0.006 g daily — 0.02 g from 10 to 14 single — 0.0075–0.01 g daily — 0.02–0.03 g Infants up to 2 years old are not given omnopon

On lengthy use of omnopon tolerance and addiction may develop Contraindications the same as for opium

Available in powder form and in ampoules containing 1 ml 1% or 2% solution

To be kept locked (List A) in tightly stoppered bottles or in sealed ampoules in a place protected from light

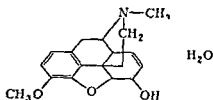
Rp Sol Omnopon 1% (2%) 10

D t d N 6 in amp

S 0.5–1 ml subcutaneously

CODEINE Codeine base (Codelinum)

Methylmorphine An alkaloid found in opium and also produced synthetically



Colourless crystals or white crystalline powder odourless bitter taste Dissolves slowly and sparingly in cold water (1:150) soluble in hot water (1:17) freely soluble in alcohol (1:2.5) in chloroform and diluted acids Melting point (after drying at 100–105°) — 154–157° The aqueous and alcoholic solutions have an alkaline reaction

Codeine is similar to morphine in its action but its analgesic properties are much weaker its ability to reduce the excitability of the cough centre is manifested quite strongly Codeine depresses respiration to a lesser degree than morphine and also inhibits gastrointestinal activity less lengthy use may nevertheless lead to constipation

Codeine is mostly used to allay coughing It is also prescribed in conjunction with hypnotics and bromides as a sedative It is an ingredient of the Bekhterev mixture

Codeine is administered orally in powders tablets and solutions the single dose for adults being 0.01–0.02 g Children are given smaller doses depending on the age

Maximal doses for adults single — 0.05 g daily — 0.2 g

Maximal doses for children 2 years old single — 0.002 g daily — 0.006 g from 3 to 4 years old single — 0.004 g daily — 0.012 g from 5 to 6 single — 0.005 g daily — 0.015 g from 7 to 9 single — 0.006 g daily — 0.02 g from 10 to 14 single — 0.006–0.01 g daily — 0.02–0.03 g Infants up to 2 years old are not given codeine

Treatment with codeine should be carried out under the observation of a physician Cases of «codeinism» — tolerance and habituation to codeine — have been reported

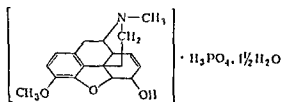
Available in powder form and in tablets of the following composition

- a) codeine — 0.015 g; sugar — 0.25 g.
- b) codeine — 0.015 g; sodium bicarbonate — 0.25 g.
- c) codeine — 0.015 g, terpin hydrate — 0.3 g;
- d) codeine — 0.02 g; powdered thermopsis herb — 0.01 g, sodium bicarbonate — 0.2 g, licorice powder — 0.2 g.
- e) codeine — 0.02 g camphor — 0.01 g, anise oil — 0.005 g, benzoic acid — 0.04 g

Tablets containing 0.01 g codeine, 0.3 g sodium bicarbonate and 0.3 g terpin hydrate are supplied under the name "Codterpin"

To be stored in tightly stoppered bottles in a place protected from light, observing safety precautions (List B)

CODEINE PHOSPHATE (Codeinum phosphoricum, Codeini phosphas).



White crystalline powder, odourless, bitterish taste. Freely soluble in water (1:35), sparingly soluble in alcohol, practically insoluble in ether and chloroform.

Similar to codeine base in action and indications for use. Since it is a less toxic drug containing as it does approximately 80% codeine base, it can be used in a higher dosage, administration to younger children is permissible.

Maximal doses for adults: single — 0.1, daily — 0.3 g.

Maximal doses for infants: from 6 months to 1 year old, single — 0.0025 g, daily — 0.0075 g; up to 2 years old, single — 0.001 g, daily — 0.012 g; children from 3 to 4 years old, single — 0.005 g, daily — 0.015 g; from 5 to 6 years old, single — 0.006–0.008 g, daily — 0.02–0.025 g; from 7 to 9 years old, single — 0.01 g, daily — 0.03 g; from 10 to 14 years old, single — 0.015–0.02 g, daily — 0.045–0.06 g.

Not prescribed for infants up to 6 months old.

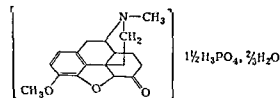
Available in powder form and in tablets of 0.015 g. Tablets of the following composition are available:

- a) codeine phosphate — 0.015 g; sugar — 0.25 g.
- b) codeine phosphate — 0.015 g, terpin hydrate — 0.25 g.
- c) codeine phosphate — 0.015 g, sodium bicarbonate — 0.25 g.

To be stored in tightly stoppered bottles in a place protected from light, observing safety precautions (List B).

HYDROCODON (Hydrocodonum)

Dihydrocodeinone. Produced synthetically from codeine. The phosphate of hydrocodon (Hydrocodonum phosphoricum) is used.



Synonyms (phosphate and bitartrate of dihydrocodeinone) Biocodone, Calmodid, Codone, Codinon, Dicodehal, Dicodeid, Hycodan, Hycodid, Hydrocodon, Mercodinone, Stodcodon Supracodin, Synkonin, Tucodil, Tuscodin

White crystalline powder, odourless, bitter taste soluble in water, insoluble in alcohol, ether and chloroform

Hydrocodon is similar to codeine in action but is more potent. Used for allaying cough in patients with various diseases of the lungs and upper respiratory passages (including among others pulmonary and laryngeal tuberculosis and cancer of the lungs). Hydrocodon often gives a favourable result where codeine is not sufficiently effective.

The drug is administered orally in tablets after meals. The dose for adults is 0.005 g 2–3 times a day. If this does not give the desired effect the single dose is raised to 0.01 g and less frequently to 0.015 g. Maximal doses for adults: single — 0.02 g, daily — 0.06 g. Children from 1 to 2 years old are given doses of 0.001–0.002 g, older children are given doses of 0.002–0.005 g.

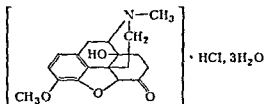
Side effects are occasionally observed after taking hydrocodon: headache, dryness in the mouth, general weakness and drowsiness. In such cases the dose should be lowered. When used over a lengthy period of time tolerance and habituation may develop.

Available in powder form and in tablets of 0.001, 0.002 and 0.005 g.

To be kept locked (List A) in tightly stoppered bottles in a place protected from light.

OXYCODONE HYDROCHLORIDE (Oxycodoni hydrochloricum)

Dihydrohydroxycodone hydrochloride



Synonyms Dihydrone, Dimarkon, Ducodal, Eubine, Eucodal, Hydrocodal, Oxykon, Stupenone, Thecodin

White crystalline powder, odourless, bitter taste. Freely soluble in water (1:6), sparingly soluble in alcohol. Solutions are sterilized for 30 min at 100°. Similar to morphine in pharmacological properties, potent analgesic, depresses the cough centre to a greater degree than codeine.

Used in place of morphine as an analgesic in pain from various causes. While as potent as morphine, oxycodone is often tolerated better by patients. It must be borne in mind that tolerance and addiction develop for oxycodone the same as for morphine.

In surgery, oxycodone is used in place of morphine in preparing patients for anaesthesia and to abolish pain in the postoperative period. Also used in obstetrics for allaying pain in labour.

Employed for allaying cough when codeine is not sufficiently effective, especially in tuberculosis patients.

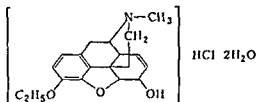
Prescribed orally in dosage of 0.005–0.01 g (for adults) 1–2 times a day. Subcutaneously 1 ml 1% solution is administered 1–2 times a day.

Maximal doses for adults (orally and subcutaneously): single — 0.01 g daily — 0.03 g.

Available in powder form, in tablets of 0.005 g and in ampoules containing 1 ml 1% or 2% solution.

To be kept locked (List A) in tightly stoppered bottles in a place protected from light.

ETHYLMORPHINE HYDROCHLORIDE (Aethylmorphinum hydrochloridum)
Obtained synthetically from morphine



Synonyms Aethylmorphin Codéthyline Diolan Dionline

White crystalline powder odourless bitter taste freely soluble in water (1/12) soluble in alcohol (1/25) slightly soluble in chloroform very sparingly soluble in ether

Ethylmorphine is similar to codeine in its general effects

Administered orally to allay coughing in chronic bronchitis pulmonary tuberculosis etc Single doses for adults — 0.01—0.02 g

Also widely used in ocular practice When ethylmorphine solutions are instilled into the conjunctival sac they cause hyperemia with subsequent anesthesia and edema of the conjunctiva Ethylmorphine relieves pain and promotes the resolution of exudates in keratitis infiltration of the cornea and inflammation of the iris as well as in other diseases Employed in ocular practice in the form of drops and ointment Treatment is begun with 1—2% solutions or ointments gradually increasing the concentration to 6, 8 or 10%

Maximal doses for oral administration (adults) single — 0.03, daily — 0.1 g

Maximal doses for children 2 years old single — 0.003 g, daily — 0.01 g from 3 to 4 years old single — 0.005 g daily — 0.015 g from 5 to 6 single — 0.006 g daily — 0.018 g from 7 to 9 single — 0.0075 g, daily — 0.025 g from 10 to 14 single — 0.01 g daily — 0.03 g Infants up to 2 years old are not given ethylmorphine

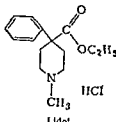
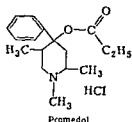
When prescribing solutions in concentrations above 8% an exclamation mark should be used to indicate that the concentration is correct

Available in powder form and in tablets of 0.01 g

To be kept locked (List A) in tightly stoppered bottles of amber glass

PROMEDOL (Promedolum)

1,2,5-Trimethyl-4-phenyl-4-propionoxyperidine hydrochloride



Synonym Trimeperidine

White crystalline powder with bitter taste freely soluble in water and chloroform soluble in alcohol insoluble in ether and benzene Solutions have at most neutral reaction they are stable on standing and are sterilized by holding at 100° for 30 min

Promedol is a potent analgetic Obtained synthetically Similar in chemical structure and pharmacological properties to the drug formerly put out under

the name of lidol (synonyms Adoban Centralgin Demerol Dolantal Dolantin Dolosal Meperidine Pethidine etc) — the hydrochloride of the ethyl ester of 1 methyl 4 phenylpiperidine-4 carbonic acid Promedol is 5–6 times more potent than lidol though there is no essential difference in toxicity

Promedol is similar to morphine in its influence on the central nervous system it diminishes the reception of pain impulses by the central nervous system and depresses conditioned reflexes Like other analgetics promedol lowers the summation capacity of the central nervous system and potentiates procaine hydrochloride and other local anesthetics It lowers the excitability of the respiratory centre and has a hypnotic effect It stimulates the centre of the vagus and the vomiting centre to a considerably less degree than morphine In experimental conditions it has a spasmolytic effect on isolated organs in the entire organism it has no significant influence on the muscles of the gut but raises the tone and intensifies the contractions of the uterine muscles

Promedol is used as an analgetic in trauma and various diseases accompanied by pain in preparing patients for operations and in the postoperative period etc Promedol is highly effective in ulcer of the stomach and duodenum cholecystitis stenocardia myocardial infarction intestinal hepatic and renal colic dyskinetic constipation and other diseases in which the pain syndrome is associated with spasms of the smooth muscles of the internal organs and the blood vessels

Promedol is widely employed in obstetrics for relieving pain and accelerating labour in ordinary doses it has no side effect on the mother or foetus

Promedol is administered subcutaneously intramuscularly and orally The analgesic effect is more pronounced when the drug is administered parenterally When necessary promedol can also be given intravenously

Orally adults are prescribed single doses of 0.025–0.05 g subcutaneously—1 ml of 1% or 2% solution

Doses of 1 ml 1% solution subcutaneously or of 0.025–0.05 g orally usually give a sufficient analgesic effect in pain of diverse origin but in cases of extreme pain particularly in patients with malignant tumours or severe trauma etc 1 ml of 2% solution is to be preferred

The drug is administered 1–3 times a day The effect comes on within 10–20 min and lasts 3–4 hrs or more after a single dose Just as in the case of other analgetics the extent and duration of analgesia may vary depending on the peculiarities of the case

Often the relief of pain is accompanied by the development of a drowsy state in patients or sleep ensues In pain associated with spasms of the smooth muscles (stenocardia and intestinal hepatic or renal colic, etc) promedol can be prescribed in combination with cholinolytic and spasmolytic drugs (atropine papaverine tifen etc)

Children are prescribed smaller doses of promedol according to their age

To allay pain in childbirth promedol is administered subcutaneously in doses of 1–2 ml 2% solution The injection is made when the cervix has dilated 1½–2 fingers the condition of the foetus being satisfactory (normal rhythm and frequency of heart contractions) if necessary the injection is repeated in 2–3 hrs The analgesic effect comes on in 10–15 min and lasts 1½–2 hrs after a single injection The use of promedol accelerates the dilation of the cervix and reduces the duration of labour a regulating influence on the motor activity of the uterus is likewise observed when labour is too violent contractions often become regular after the administration of promedol Promedol can be combined with other analgetics in relieving pain during childbirth A. M. For recommends the injection of 3 ml 1% promedol with 0.5 ml 1% oxy codon hydrochloride

There have been reports of the successful use of promedol for relieving pain during labour by administering 3 ml 1% solution mixed with 5–10 ml of blood from the patient's vein The analgesic effect lasted from 4 or 5 to 8 hrs (N. P. Verkhatsky)

Promedol can also be used in combination with other drugs, it is often used in combination with chlorpromazine as an ingredient of "lytic mixtures" (see p 27)

Maximal doses for adults orally single — 0.06 g, daily — 0.12 g
Subcutaneously single — 0.04 g daily — 0.08 g

Maximal doses for children 2 years old, single, orally — 0.005 g, subcutaneously — 0.003 g, daily, orally — 0.01 g, subcutaneously — 0.006 g
From 3 to 4 years old single, orally — 0.0075 g, subcutaneously — 0.005 g, daily, orally — 0.015 g, subcutaneously — 0.01 g
From 5 to 6 single, orally — 0.01 g subcutaneously — 0.0075 g daily, orally — 0.02 g, subcutaneously — 0.015 g
From 7 to 9 single, orally — 0.01 g, subcutaneously — 0.0075 g daily orally — 0.02 g subcutaneously — 0.015 g
From 10 to 14 single orally — 0.015 g, subcutaneously — 0.01 g daily orally — 0.03 g, subcutaneously — 0.02 g
Infants up to 2 years old are not given promedol

Promedol is usually tolerated well. In rare cases slight nausea may be observed, and at times vertigo, weakness and a feeling of mild intoxication. These symptoms pass away of themselves. If side effects should be observed on repeated administration of the drug, the dose should be lowered.

When promedol is used for lengthy periods the development of tolerance and habituation may occur.

Promedol is contraindicated when the respiration is depressed.

Available in powder form, in tablets of 0.025 g and in ampoules containing 1 ml 1% or 2% solution.

To be kept locked (List A) in tightly stoppered bottles or sealed ampoules. To be issued and used with the same restrictions as morphine and similar drugs.

Rp Promedoli 0.025

D t d N 6 in tabul

S 1 tablet twice a day

Rp Sol Promedoli 2% 10

D t d N 6 in amp

S 1 ml subcutaneously twice a day

Escodol (Escodolum) Combined preparation ready for use, aqueous solution in ampoules 1 ml containing 0.02 g promedol, 0.0005 g scopolamine and 0.025 g ephedrine.

Similar in action to the foreign drug scophedal (S. E. E.), which contains scopolamine, oxycodone hydrochloride and ephedrine.

Used in surgical practice alone and in combination with chlorpromazine for medicamentous preparation and basal anesthesia in local and general anesthesia (I. S. Zhorov).

Administered subcutaneously and intramuscularly.

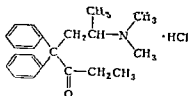
Doses should be individualized, taking into consideration the patient's general condition and weight, as well as the possibility of different sensitivity to the drug (especially due to the scopolamine content — see p 101).

Dosage for adults 0.75—1 ml

To be kept locked (List A) in sealed ampoules in a place protected from light.

PHENADONE (Phenadonum)

6 Dimethylamino 4,4 diphenylheptane 3 one hydrochloride



Synonyms Adanon, Algidon, Algil, Algolysin, Algoxale, Amidon, Amid osan, Anadon Butalgin Depridol, Diaminone, Dianone, Dolafin, Dolamid Dolesone, Dolophine, Dorexol, Heptadon, Heptanal, Heptanone, Ketalgin, Me codin, Mepecton Mephenon, Methadone, Miadone, Moheptan, Physerton, Pol amidon, Sin Algin, Sintalgon, Symoron, Turanone, Vermonyl

White crystalline powder, odourless, soluble in water, alcohol and chloro form insoluble in ether

Phenadone is a potent analgesic and possesses spasmolytic properties it may cause euphoria The toxicity is higher than that of other synthetic morphine substitutes (e g promedol), and it is therefore prescribed in smaller doses

Used in cases of pain associated with spasms of the smooth muscles of the internal organs and blood vessels (in ulcer of the stomach and duodenum, cholecystitis intestinal colic stenocardia), in neuralgic pain etc

Administered orally The single dose for adults is 0.003—0.005 g Can be given 2—3 times daily In order to increase the spasmolytic and analgesic effect it is recommended that phenadone should be prescribed simultaneously with tipher papaverine or other spasmolytics

Maximal doses (for adults) single—0.01 g daily—0.03 g

Possible complications nausea, vertigo and vomiting

Contraindicated for the aged and for infants, and in cases of insufficiency of the respiratory centre.

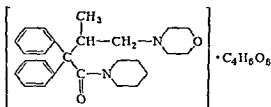
Lengthy use may lead to tolerance and habituation

Available in powder form

To be kept locked (List A) in well closed bottles of amber glass in a place protected from light The same restrictions must be observed in dispensing as in the case of morphine

DEXTROMORAMIDE (Dextromoramidum)

D (+) 2,2 diphenyl-3 methyl 4 morpholinobutyl pyrrolidine bitartrate¹



Synonyms Errecalma, Palfium, Pyrrolamidol, Troxilan

Similar to phenadone in chemical structure and action, potent analgesic Employed in cases of acute and chronic pain, especially in trauma, postoperative pain and malignant neoplasms

Prescribed subcutaneously in dosage of 1 ml solution containing 0.0069 g of the drug (the equivalent of 5 mg of the base) or 0.0138 g (10 mg of the base) Also administered orally in tablets containing 0.0069 g (5 mg of the base) and rectally in suppositories of 0.0138 g (10 mg of the base)

In some cases dextromoramide has an analgesic effect where other analgesics are ineffective

Side effects may be observed when the drug is used vertigo nausea presyncopic condition These symptoms are usually associated with overdosage Under ordinary conditions intravenous administration is impermissible since serious complications are possible depressed respiration and collapse Because of its pronounced depressing effect on the respiration dextromoramide must

¹ Lately the term «hydrotartrate» has also begun to be used instead of «bitartrate»

not be used in combination with other drugs that depress the respiratory centre analgesics and barbiturates

Lengthy use of dextromoramide may lead to tolerance and habituation

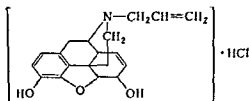
To be stored and dispensed with the same precautions and restrictions as morphine

Dextromoramide is a foreign drug which has been tested with favourable results in the USSR and approved for use in medical practice by the Pharmacological Committee

B. Antagonists of morphine and other analgetics

ANTORPHINE. Nalorphine (Antorphinum Nalorphini hydrochloridum)

Allynormorphine hydrochloride



Synonyms Lethidron Nalline

White crystalline substance freely soluble in water Melting point 258—260°

Antorphine is similar to morphine in chemical structure the only difference being the presence of an allyl instead of a methyl radical attached to the nitrogen atom. In its pharmacological properties antorphine differs significantly from morphine. The depression of respiration lowering of the arterial pressure arrhythmia and other changes in body activities caused by morphine and other analgetics (promedol isopromedol phenadone dextromoramide, etc) are overcome by antorphine. Antorphine does not have an antagonistic action in depression of respiration and disorders of the circulation caused by barbiturates cyclopropane and ethyl ether.

Antorphine is employed as an antidote in cases of sharp depression of respiration due to an overdosage of morphine promedol or other analgetics or to a heightened sensitivity to them. It is not used for the treatment of chronic morphinism.

Antorphine is also used for the prevention and treatment of asphyxia neonatorum when pain during childbirth is allayed with analgetics.

Antorphine is administered intravenously intramuscularly or subcutaneously. Intravenous administration is the most effective. Adults are prescribed 0.005—0.01 g (1—2 ml of 0.5% solution). If the effect is inadequate injections are repeated at intervals of 10—15 min. The total dose should not exceed 0.04 g (40 mg).

When there is danger of respiration being depressed in the newborn infant women in labour are given a subcutaneous injection of the drug approximately 10 min before delivery.

Newborn infants are given an injection of 0.0001—0.00025 g (0.2—0.5 ml of 0.05% solution) into the umbilical vein. If necessary injections can be repeated at intervals of 1—2 min but the total dose should not exceed 0.0003 g (0.8 mg).

The administration of antorphine ordinarily causes no side effects but large doses may give rise to nausea, muosis, drowsiness and headache.

The administration of antorphine to morphine addicts may cause a characteristic attack of abstinence symptoms.

Available in ampoules containing 1 ml 0.5% solution (for adults) or 0.5 ml of 0.05% solution (for newborn infants).

C. Analgetics, febrifuges and antiphlogistics — derivatives of salicylic acid, pyrazolone and aniline

a) Derivatives of salicylic acid

SODIUM SALICYLATE (Natrium salicylicum, Natrii salicylas)

Synonym Nadisal



White crystalline powder or small scales odourless, sweetish salt taste. Freely soluble in water (1 : 1), soluble in alcohol (1 : 6) and in glycerol (1 : 5), insoluble in ether. Solutions are sterilized by holding at 100° for 30 min.

Sodium salicylate, like other salicylates, possesses analgesic properties. These drugs also have a characteristic influence on thermal regulation, and lower the temperature in febrile diseases. This effect is preeminently associated with their action on the corresponding centres of the brain.

The salicylates have a less pronounced analgesic action than the opium alkaloids and their synthetic analogues, they are only slightly effective in acute pain, trauma, etc. They do not cause euphoria and have no hypnotic effect, they do not depress the cough and respiratory centres.

An important property of the salicylates is their antiphlogistic action. They have a stimulating influence on the hypophysis and the adrenal cortex and cause a distinct rise in the content of 17 hydroxycorticosteroids in the blood. Under their influence the activity of hyaluronidase is diminished and the permeability of the capillaries lowered. The action of the salicylates has some similarity to that of the adrenocorticotrophic hormone of the hypophysis.

Due to the pharmacological properties of the salicylates noted, they are successfully used in treating rheumatism, non-rheumatic arthritis, exudative pleuritis and other diseases accompanied by an active inflammatory reaction, they are also employed in various diseases that proceed with a febrile reaction in neuralgia, myalgia, headache and chorea.

Sodium salicylate is usually prescribed orally in doses of 0.5–1 g for adults and 0.1–0.5 g for children.

In cases of acute rheumatism, rheumatic endocarditis and myocarditis adults are prescribed large doses during the first days of treatment (up to 8 or 10 g daily, in doses of 1–2 g every 2–3 hrs). Sometimes intravenous administration is resorted to, particularly in rheumatic endocarditis (from 3–5 up to 10 ml of 10 or 15% solution daily over a period of 10–15 days), sometimes 3, 5 or 10 ml of 40% methenamine solution is administered simultaneously. Intravenous injections must be performed slowly. In sharp attacks of rheumatism, children are prescribed 0.5 g in 24 hrs for each year of their age, but the total daily dose must not exceed 6 g. Treatment of rheumatism with salicylates is lengthy. Administration of the drug in large doses is continued after the temperature has been lowered and inflammatory symptoms have abated, then the dose is gradually lowered (to 3–4 g daily for adults). The length of treatment with salicylates depends on the peculiarities of the case.

Side effects may be observed when sodium salicylate is given: nausea, vomiting, a roaring in the ears, impairment of hearing, excessive sweating, angioneurotic edema, hallucinations, etc. A heightened sensitivity to salicylates has been noted in individuals suffering from bronchial asthma. Allergic reactions are possible (rash, etc.).

In order to lessen dyspeptic manifestations, it is recommended that sodium salicylate should be taken after meals and drunk down with milk, or prescribed in capsules

Side effects can be diminished by taking sodium bicarbonate, the latter, however, facilitates the more rapid excretion of salicylates and is therefore usually not recommended. It has been reported that dyspeptic symptoms abate under the influence of nicotinic acid (0.05—0.1 g 2—3 times a day)

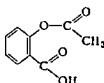
Salicylates cause some reduction in the prothrombin content of the blood, an opinion has been advanced as to the possibility of using sodium salicylate as a weak anticoagulant (S. V. Shestakov). Recent investigations have shown that the bleeding time and the number of platelets in the blood do not change after ordinary doses of sodium salicylate or aspirin (M. N. Malova), and that when used in conjunction with anticoagulants, salicylates do not influence the return of prothrombin to the initial level after the withdrawal of the anticoagulant (R. I. Averina). It must nevertheless be borne in mind that in cases of impaired coagulation of the blood especially in hemophilia, salicylates may promote the development of hemorrhage (Quick et al). At the same time it should be pointed out that different salicylates have a different influence on the prothrombin content, salicylamide having the least effect.

Sodium salicylate is available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well closed bottles in a dry place protected from light

ASPIRIN (Aspirinum)

Acetylsalicylic acid (Acidum acetylsalicylicum)



Synonyms: Acesal, Aceticyl, Acetol, Acetophen, Acetosol, Acetylin, Acetyl sal, Acetylpyrin, Aspro, Empirin, Genasprin, Helicon, Istopyrin, Polopiryna, Rhodine, Salacetin, Salatin.

White needles or platelets, faintly acid taste, sparingly soluble in water, freely soluble in solutions of sodium hydroxide and sodium carbonate. Aqueous solutions have an acid reaction. Melting point 133—136°.

In its pharmacological properties and mode of action, aspirin is similar to sodium salicylate but it causes dyspeptic symptoms less frequently and is tolerated better. It has nevertheless been reported that aspirin may cause bronchial spasm. In its antiphlogistic action and its effectiveness in rheumatism, aspirin is somewhat inferior to sodium salicylate.

Employed orally in neuralgia, migraine and febrile diseases in a dosage of 0.25—0.5 g or 1 g 3—4 times a day. In acute rheumatism and rheumatic endo- and myocarditis 4—5 g daily is given.

Single doses for children: up to 1 year old — 0.05 g, 2 years — 0.1 g, 3—4 years — 0.2 g, 5—6 years — 0.25 g, 7 years — 0.3 g, 8—14 years — 0.3—0.5 g.

Available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well closed bottles

Aspirin is an ingredient of the compound tablets "Asphen", "Ascophen", "Novocephalin" and "Citramon". Compound tablets of the following composition are also available: a) aspirin 0.5 g, caffeine sodium benzoate 0.2 g, b) aspirin 0.3 g, caffeine sodium benzoate 0.1 g, c) aspirin 0.25 g, caffeine 0.05 g, d) aspirin 0.25 g, phenacetin 0.25 g, caffeine 0.05 g.

Rp Aspirini 0.25

D t d N 6 in tabul

S 1 tablet 3 times a day

Rp Aspirini 05
 Coffeini 005
 D t d N 6 in tabul
 S 1 tablet 2—3 times a day

Rp Aspirini
 Phenacetini \overline{aa} 025
 Coffeini natrio benzoici 01
 D t d N 6 in tabul
 S 1 tablet 2—3 times a day (in migraine and neuralgia)

Rp Aspirini
 Phenacetini \overline{aa} 025
 Codeini phosphorici 001
 M. f. pulv. D t d N 6
 S 1 powder 3 times a day (in migraine and neuralgia)

Ascophen (Ascophenum) Tablets containing 02 g aspirin 02 g phenacetin and 004 g caffeine

Asphen (Asphenum) Tablets containing 0.25 g aspirin and 0.15 g phenacetin

Novocephalgin (Novocephalginum) Tablets containing 03 g aspirin 02 g phenacetin and 003 g caffeine

Citramon (Citramonum) Tablets or powders containing 024 g aspirin 018 g phenacetin 003 g caffeine 003 g cocoa 002 g citric acid and 05 g powdered sugar

All these tablets are used in headache neuralgia colds etc Prescribed in dosage of 1 tablet 2—3 times a day

SALICYLAMIDE (Salicylamidum)

The amide of salicylic acid



Synonyms Algamon Salamide Salamid

White crystalline powder sparingly soluble in water soluble in alcohol
 Melting point 140—142°

Salicylamide is similar to sodium salicylate and aspirin in chemical structure and influence on the body but it also has a number of peculiar properties. It is more stable than aspirin which is easily hydrolyzed in the body with the formation of salicylic acid. Salicylamide is hydrolyzed with difficulty and is excreted unchanged in considerable amounts. Unlike other salicylates salicyl amide has no marked influence on the prothrombin content in the blood nor does it cause dyspeptic symptoms.

Indications for use are the same as for sodium salicylate and aspirin. It is prescribed orally as an analgetic and febrifuge in a dosage of 0.25—0.5 g 2—3 times a day. In rheumatism it is given in doses of 1 g 6, 8 or 10 times a day. In acute attacks of rheumatism, children are given 0.4, 0.5 or 0.6 g daily for each year of their age.

Nausea and vertigo may be observed when the drug is used and at times pain in the region of the stomach. In order to diminish side effects the drug should be taken after meals and drunk down with copious amounts of liquid. In some cases salicylamide is tolerated better than sodium salicylate or aspirin.

Available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well-closed bottles

METHYL SALICYLATE (Methylum salicylicum)



Colourless or yellowish liquid characteristic aromatic odour, practically insoluble in water miscible with alcohol and ether in all proportions Specific gravity 1.178—1.186

Applied externally per se and mixed with chloroform and fatty oils as an analgesic and antiphlogistic liniment in articular and muscular rheumatism arthritis and exudative pleuritis

To be stored in well stoppered bottles in a dark place

Rp Methyl salicylic

Chloroformil āā 100

Ol Hyoscyami 300

MDS For external use to be rubbed in

Available ready for use in packages of 50 g under the name "Saliniment"

Rp Methyl salicylic 100

Trae Capsici

Ol Hyoscyami āā 200

MOD For external use to be rubbed in

Available ready for use in packages of 50 g under the name "Capsin"

Rp Menthol 40

Methyl salicylic 210

Vaselin 750

M f ung

DS For external use to be rubbed in

Available ready for use under the name "Baume Benguê"

Rp Methyl salicylic 240

Ol Eucalypti 12

Ol Terebinthinae 32

Camphorae tritae 50

Axungiae porcinae

Vaselin āā 333

M f ung

DS For external use to be rubbed in

Available ready for use under the name "Balsam Sanitas"

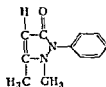
Analgesic emulsion. Composition methyl salicylate 25 parts analgin 25 parts naphthalan petroleum 25 parts emulsifier 75 parts water up to 100 parts

Used as a liniment in rheumatism, neuralgia etc

b) Derivatives of pyrazolone

ANTIPYRINE (Antipyrinum)

1 Phenyl 2,3 dimethyl 5 pyrazolone



Synonyms Analgesin Anodynin Azophenum Methozin Parodyn Phenazonum Phenylen Phenylon Pyrazin Pyrazolin Pyrodin Sedatin

Colourless crystals or white crystalline powder odourless very freely soluble in water (1:1) and in chloroform freely soluble in alcohol sparingly soluble in ether Melting point 110–113° Solutions are sterilized by holding at 100° for 30 minutes

Antipyrine is one of the pyrazolone derivatives — drugs having an analgesic effect In their analgesic and antipyretic potency these compounds are similar to derivatives of salicylic acid

An important property of the pyrazolone derivatives is their ability to reduce the permeability of the capillaries increase their stability and hinder the development of an inflammatory reaction

The mode of this action has not been completely explained Unlike the salicylates these compounds have no marked effect on the hypophysis — adrenal system

Of the pyrazolone derivatives employed in medical practice antipyrine has the weakest antiphlogistic effect aminopyrine analgin and butadion are considerably more potent particularly the latter

Antipyrine has a moderate hemostatic effect

Antipyrine is employed in neuralgia rheumatism chorea and colds

Prescribed orally for adults in a dosage of 0.25–0.5 g Infants from 6 to 12 months old are given 0.03–0.05 g Children from 2 to 5 years 0.1–0.2 g from 6 to 12 years 0.2–0.25 g These doses are given 2–3 times a day

Maximal doses for adults single — 1 g daily — 3 g

Maximal doses for children from 6 months to 1 year single — 0.05 g daily — 0.15 g 2 years single — 0.075 g daily — 0.2 g 3–4 years single — 0.1 g daily — 0.3 g 5–6 years single — 0.15 g daily — 0.45 g 7–9 years single — 0.2 g daily — 0.6 g 10–14 years single — 0.25–0.3 g daily — 0.75–0.9 g Infants up to 6 months old are not prescribed antipyrine

As a hemostatic agent a 10–20% solution of antipyrine is sometimes used for moistening tampons and napkins in nasal and parenchymatous hemorrhage

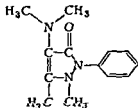
When prescribing antipyrine one must bear in mind the possibility of heightened sensitivity to the drug with the appearance of urticaria and fixed rash

Available in powder form and in tablets of 0.25 g

To be stored in well stoppered bottles in a place protected from light observing safety precautions (List B)

AMINOPYRINE (*Aminopyrinum*)

Dimethylamino antipyrine or 1 phenyl 2,3 dimethyl 4 dimethylamino 5 pyrazolon



Synonyms Alamidon Amidazophen Amidofebrin Amidopyrazoline Amidopyrinum Amidozon Aminophenazon Aminopyrazolin Anafebrina Aneuxol Dimapyrin Dimethylaminophenazon Dipyrin Novamidon Pyradone Pyramidon Pyramin Pyrazon Pyrazorin Stellamidon

White crystals or white crystalline powder with barely perceptible yellowish tint odourless faintly bitter soluble in water (1:20) and in ether freely soluble in alcohol (1:2) very freely soluble in chloroform Melting point 107–109° Solutions are sterilized by holding at 100° for 30 min pH of 2 and 4% solutions — 7.0–7.8

Aminopyrine is an antipyretic, analgetic and antiphlogistic. In the character of its action it is similar to antipyrine but 2—3 times more potent.

Used in headache, neuralgia, arthritis, myositis and chorea. Often employed in acute articular rheumatism.

Prescribed orally in powders and tablets, less frequently in solutions. In doses of 0.25—0.3 g 3—4 times a day. In acute attacks of rheumatism 2—3 g daily is prescribed.

Infants from 4 to 12 months old are prescribed doses of 0.025—0.05 g. Children from 2 to 5 years old 0.05—0.1 g, from 6 to 12 years 0.1—0.15 g. In rheumatic polyarthritis the single dose is increased 50—100% (approximately 0.15 g daily for each year of age given in 4 doses).

Maximal doses for adults: single — 0.5 g daily — 1.5 g.

Maximal doses for children up to 6 months old: single — 0.025 g daily — 0.075 g, from 6 months to 2 years: single — 0.05 g daily — 0.15 g, 3—4 years: single — 0.075 g daily — 0.2 g, 5—6 years: single — 0.1 g daily — 0.3 g, 7—9 years: single — 0.15 g daily — 0.45 g, 10—14 years: single — 0.2—0.3 g daily — 0.6—0.9 g. When treating rheumatism it is permissible to increase the daily dose to 0.15—0.2 g per year of age.

When treating with aminopyrine over a lengthy period of time the blood must be examined periodically since in isolated cases a depression of hemopoiesis may be observed (granulocytopenia and agranulocytosis). Rashes sometimes develop.

Available in powder form in tablets of 0.25 g and in ampoules containing 2—5 and 10 ml of 2% solution and 10 ml of 4% solution.

Aminopyrine is often prescribed along with phenacetin, antipyrine, phenobarbital, barbitol, caffeine and other drugs.

Compound tablets of the following composition are available: a) aminopyrine 0.25 g, caffeine sodium benzoate 0.1 g; b) aminopyrine 0.3 g, caffeine 0.05 g; c) aminopyrine 0.25 g, analgin 0.25 g; d) aminopyrine 0.25 g, analgin 0.25 g, caffeine sodium benzoate 0.1 g, as well as others (see also Phenobarbital p. 9 and Phenacetin p. 59).

Aminopyrine is to be stored in well stoppered bottles in a place protected from light, observing safety precautions (List B).

Verodon (Verodonum). Tablets (0.4 g) containing aminopyrine and barbitol in molecular proportion of 1:2. Used as an analgetic, sedative and hypnotic. Prescribed in dosage of 1 tablet 2—3 times a day.

Pyraphen (Pyraphenum). Tablets containing 0.25 g aminopyrine and 0.25 g phenacetin.

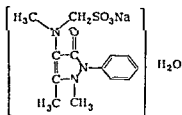
Pyraminal (Pyraminalum). Tablets containing 0.25 g aminopyrine, 0.03 g caffeine and 0.02 g phenobarbital.

Pyramein (Pyrameinum). Tablets containing 0.3 g aminopyrine and 0.03 g caffeine.

Novomigrophen (Novomigrophenum). Tablets containing 0.2 g aminopyrine, 0.1 g phenacetin, 0.015 g caffeine, 0.015 g citric acid and 0.1 g sugar.

All these tablets are used for headache, neuralgia and colds, prescribed in dosage of 1 tablet 2—3 times a day.

ANALGIN (Analginum)



1-Phenyl 2,3 dimethyl 5-pyrazolone 4 methylamino methylene sodium sulfo
nate

Synonyms Algyrin, Analgetin, Cibalgin, Dipyrin, Metamizol, Metapyrin, Methylmelubrin, Minalgin, Neomelubrin Novaldin, Novalgin, Novamidazophen, Novaminosulfon, Novapyrin; Pantalgan, Pyralgin, Pyretin, Pyridone, Pyrisan, Salpyrine, Sulfonovin, Zymapiril

White or slightly yellowish crystalline powder, freely soluble in water (1:1.5), sparingly soluble in alcohol, insoluble in ether. Aqueous solutions are sterilized by holding at 100° for 30 min. pH of 50% solution 6.3–7.3. Solutions quickly turn yellow.

Analgin possesses very marked analgesic, antiphlogistic and antipyretic properties. In the character of its action, analgin is similar to aminopyrine as a freely soluble drug which is easily absorbed, it is especially convenient for use when necessary quickly to create a high concentration in the blood. Analgin's high solubility makes possible its wide application for parenteral administration. Solutions do not irritate the tissues even in high concentrations.

The simultaneous administration of analgin and aminopyrine makes it possible to achieve a rapid therapeutic effect because of the quick entry of analgin into the blood stream, as well as a lengthy effect as a result of the slower absorption and excretion of aminopyrine. Analgin is used in pain of diverse origin (headache, neuralgia, radiculitis, myositis), fevers, influenza, rheumatism and chorea. Prescribed orally for adults in a dosage of 0.25–0.5 g 2–3 times a day. In articular and muscular rheumatism 0.5–1 g is given 3 times a day. In severe pain, 1 ml of 50% solution is injected subcutaneously, intramuscularly or intravenously 2–3 times a day.

Maximal doses for adults: single — 1 g; daily — 3 g.

Children are prescribed analgin orally in the following doses: up to 2 years old, 0.025–0.05 g, 3–4 years, 0.1 g, 5–6 years, 0.15 g, 7 years, 0.2 g, 8–14 years, 0.25–0.3 g.

Parenterally, children are given a 50% solution 1–2 times a day in the following doses: up to 2 years old, 0.1 ml, 3–4 years, 0.2 ml, 5–6 years, 0.3 ml, 7 years, 0.4 ml, 8–14 years, 0.5–0.6 ml.

Maximal doses for children: from 6 months to 1 year old, single — 0.05 g, daily — 0.15 g, 2 years, single — 0.1 g, daily — 0.3 g, 3–4 years, single — 0.15 g, daily — 0.45 g, 5–6 years, single — 0.2 g, daily — 0.6 g, 7–9 years, single — 0.25 g, daily — 0.75 g, 10–14 years, single — 0.3–0.5 g, daily — 0.9–1.5 g. Infants up to 6 months old are not prescribed analgin.

Available in powder form, in tablets of 0.5 g and in ampoules containing 1 ml 50% solution.

To be stored in well closed bottles in a place protected from light, observing safety precautions (List B).

Rp Analgin 0.5
D t d N 10 in tabul
S 1 tablet 2–3 times a day

Rp Analgin
Pyramidon \overline{aa} 0.25
D t d N 6 in tabul
S 1 tablet 2–3 times a day

Rp Analgin
Pyramidon \overline{aa} 0.25
Coffein natrio benzoici 0.1
D t d N 10 in tabul
S 1 tablet 2–3 times a day

Rp Analgin
Phenacetin \overline{aa} 0.25
Coffein natrio benzoici 0.25

Codein: 0015

D t d N 10 in tabul

S 1 tablet 2—3 times a day

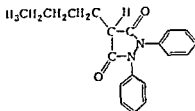
Rp Sol Analgin 50% 10

D t d N 6 in amp

DS 1 ml intramuscularly 1—2 times a day

BUTADION (Butadionum)

1 2 Diphenyl 2 n butyl 3 5 pyrazolidine dione



Synonyms Artrizin Butalidon Butapirazol Butartril Butazolidin Butyl pyrin Phebuzine Phenopyrine Phenylbutazonum Pyrazolidin

White crystalline powder bitter, practically insoluble in water, soluble in dilute solutions of alkalis Melting point 105° The sodium salt of butadion is freely soluble in water

Butadion has an analgesic antipyretic and antiphlogistic effect, considerably superior to amnopyrine and salicylates in its antiphlogistic properties Like other derivatives of pyrazolone its antiphlogistic action is not directly associated with an influence on the hypophysis and adrenals

The drug is quickly absorbed and remains in the blood for a relatively long period of time

Butadion is used for the treatment of acute forms of rheumatism acute subacute and chronic rheumatoid polyarthritis infectious nonspecific polyarthritis Bekhterev disease gout psoriatic arthritis erythema nodosum

Butadion can be used alone and in combination with hormone preparations (Cortisone Prednisone etc)

In arthritis of diverse etiology butadion quickly abates the pain and inflammatory reaction it also quickly aborts attacks of gout and reduces the uric acid content in the blood It has been reported that butadion is effective in thrombophlebitis of the lower extremities and hemorrhoidal veins that the use of the drug causes an abatement of pain edema and hyperemia and leads to a substantial improvement in the general condition There have also been reports that butadion has a favourable effect in lupus erythematosus A good result has been observed in iridocyclitis (abatement of exudation and pain)

Butadion is prescribed orally during or after meals The single dose for adults is 0.1—0.15 g the drug is taken 4—6 times a day the daily dose amounting to 0.45—0.6 g When a noticeable improvement has set in the dose can gradually be reduced to 0.2—0.3 g daily Children are prescribed butadion in smaller doses 0.05 0.075 or 0.1 g 3—4 times a day depending on the age The course of treatment totals 2—5 weeks

Butadion has been used in lymphogranulomatosis Administration of the drug in a dosage of 0.15 g 2—4 times a day over a period of 21—90 days caused a fall in the temperature and a diminution of pain and in some cases promoted remission The effect of butadion in lymphogranulomatosis is not specific but it can be used for patients in whom treatment with roentgen rays or the motherapeutic agents (see Novembichin Dopan) is contraindicated or ineffective (Z G Aprosina N V Belyaeva)

Side effects may be observed during treatment with butadion: nausea, vomiting, pain in the region of the stomach (due to the drug's irritating action and the increased secretion of gastric juice), frequent stool, rash, leukopenia (to extent of agranulocytosis) and anemia and hemorrhagia (especially hematuria). In individuals with a heightened sensitivity to butadion it is expedient after 2-3 days treatment with the usual doses gradually to reduce the dose to 5-0.3 g daily. Treatment must be carried out under careful medical observation. The blood must be examined at least every 5-7 days.

In order to lessen dyspeptic symptoms, antacid agents that do not contain calcium can be prescribed (e.g. magnesium trisilicate). A reduction in the number of leukocytes in the blood or other hematological changes, as well as allergic reactions are indications for withdrawal of the drug.

Butadion is contraindicated in ulcer of the stomach and duodenum (because of the possibility of gastric hemorrhage), in diseases of the hematogenic organs, impairment of the liver and kidney functions and decompensated cardiac activity. When prescribing butadion it is recommended that the intake of sodium chloride should be limited so as to avoid the retention of water and the development of edema. In order to lessen the irritating effect on the mucous membrane, the drug should not be prescribed in powder form, but given as tablets or capsules. When butadion is prescribed along with other medicines, it must be borne in mind that it can delay the excretion by the kidneys of certain drugs (aminopyrine, morphine, PAS, penicillin etc.) and in this way lead to their accumulation in the body and the possible development of side effects.

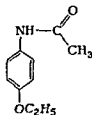
Available in powder form (for making tablets or filling capsules) and in tablets of 0.05 and 0.1 g.

To be stored in a place protected from light, observing safety precautions (see B).

c) Derivatives of aniline

PHENACETIN (Phenacetinum)

Para acetphenetidin



Synonyms: Acetophenetidin, Acetophenidin, Acetparaphenylide, Phenetidin, Phenin.

White, fine crystalline powder, odourless, slightly bitter, very sparingly soluble in water, sparingly soluble in boiling water (1:70), soluble in alcohol (1:16), soluble in chloroform. Solutions have an acid reaction. Melting point 136°.

Phenacetin has an antipyretic, analgesic and antiphlogistic effect.

Used in neuralgia, headache and inflammatory diseases, either alone or in combination with other agents (caffeine, aminopyrine, antipyrine, codeine, etc.) prescribed orally: adults, in doses of 0.2-0.5 g; children from 6 to 12 months 0.03-0.05 g, from 2 to 5 years, 0.1-0.15 g; from 6 to 12 years, 0.15-0.3 g. These doses are given 2-3 times a day.

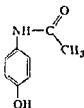
Phenacetin is usually tolerated well, in isolated cases allergic skin reactions are possible (urticaria, etc.). In large doses phenacetin may cause methemoglobinemia.

Available in powder form and in tablets of 0.25 g. Phenacetin is an ingredient of the tablets "Pyraphen" and "Novomigrophen". Compound tablets of

the following composition are also available a) phenacelin 0.25 g, caffeine 0.05 g b) phenacelin 0.25 g, aminopyrine 0.25 g, caffeine 0.05 g, c) phenacelin 0.25 g aminopyrine 0.25 g, caffeine sodium benzoate 0.1 g, d) phenacelin 0.25 g, aspirin 0.25 g, caffeine 0.05 g

ACETAMINOPHENOL (Acetaminophenolum)

Para acetaminophenol



Synonyms Acetaminophen Acetophen Algotropyl, Alvedon, Apamide, Dolamin Febridol, Fendon Panadol Paracetamol, Tempra, Traigon, Tylenol

White crystalline powder insoluble in water Melting point 167—168°

In structure and action acetaminophenol is similar to phenacelin, but somewhat less toxic judging by information in the literature it does not cause the formation of methemoglobin Used as a febrifuge, analgetic and antiphlogistic the indications being the same as for phenacelin Can be used in combination with aminopyrine, caffeine, phenobarbital and other drugs

Doses for adults single, 0.2, 0.3, 0.5 g, daily, 0.8—1.2 g Children are prescribed the following doses from 6 to 12 months old, 0.03—0.05 g, from 2 to 5 years 0.1—0.15 g, from 6 to 12 years, 0.15—0.25 g These doses are given 2—3 times a day

Available in powder form and in tablets of 0.1, 0.15 and 0.25 g.

To be stored in well stoppered bottles, observing safety precautions (List B)

IV. ANTICONVULSANTS

Various substances may have an anticonvulsive effect, either by intensifying inhibitory processes or by weakening excitatory processes in the central nervous system

Convulsions can also be prevented or stopped by means of agents that depress the transmission of stimuli in the region of the endings of the motor nerves (drugs of the curare group see p 123)

The following drugs are widely used as anticonvulsants bromides, magnesium sulphate chloral hydrate, and the barbiturates, particularly phenobarbital the latter along with its hypnotic action, greatly lowers the excitability of the motor centres of the brain

Today medicinal substances are available which are capable, by their influence on the central nervous system of suppressing spasmodic reactions more selectively without having a general depressing action and in particular, without having a hypnotic effect Among these compounds are some derivatives of hydantoin, oxazolindione etc These substances have found wide application in the treatment of epilepsy It is important to note that some of them (e.g. diphenylhydantoin) are preeminently effective in major attacks of epilepsy (grand mal) while others (e.g. trimethine) are effective in minor attacks (petit mal)

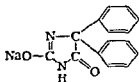
New compounds have also been synthesized lately which diminish convulsive manifestations and lower the muscular tone in parkinsonism and other diseases associated chiefly with an affection of the subcortical elements of the central nervous system. In treating these diseases use has long been made of

atropine and scopolamine and preparations containing the total alkaloids of digitalis (infusions and extracts) A characteristic pharmacological property of these alkaloids is their cholinolytic action, that is, their ability to lower the sensitivity of the organs and tissues to acetylcholine, which is the chemical transmitter (mediator) of the neural impulse

The action of the digitalis alkaloids is, however, manifested particularly strongly in respect to the peripheral cholinoreactive systems, and to a less degree in respect to the cholinoreactive systems of the central nervous system. It has recently been established that compounds having a more pronounced central cholinolytic action are more effective in the treatment of parkinsonism under experimental conditions these compounds weaken or prevent the convulsive reaction caused in animals by nicotine and arecoline. Among drugs of this type are tropacin, diethazine, etc. They are widely employed today in treating parkinsonism, Parkinson's disease and other so called "extrapyramidal diseases". According to present conceptions their therapeutic effect is associated to a certain degree with a lowering of the sensitivity of the synapses of the central nervous system to acetylcholine

A. Substances used in the treatment of epilepsy

DIPHENYLHYDANTOIN SODIUM (Diphenylhydantoinum natrium)
55 Diphenylhydantoin sodium



Synonyms Alepsin, Antisacer, Cansoin, Citrullamon, Comital, Denyl sodium, Dihydan, Dilantin sodium, Dintoin, Diphedal, Diphedan, Diphenin, Diphentoin, Epanutin, Epifenyl, Epilan D, Eptal, Eptoin, Hydantal, Hydantoinalum, Idantoin, Lepitoin, Oxylan, Phenytolnum, Silantin sodium, Sodanton, Solantoin, Solantyl, Zentrinal, Zentropil

White crystalline powder with yellowish tint, odourless, slightly bitter, freely soluble in water, insoluble in ether and chloroform. On long contact with the air decomposes with the formation of diphenylhydantoin. Instead of sodium diphenylhydantoinate, a mixture of diphenylhydantoin and the equivalent amount of sodium bicarbonate is also used, this is available in tablets of 0.1 g.

Diphenylhydantoin sodium is an anticonvulsant which has no hypnotic effect. It is used in treating epilepsy, principally major convulsive attacks.

Diphenylhydantoin sodium is administered orally. In order to avoid irritating the stomach because of the alkaline reaction it is taken in capsules after meals. Doses should be individualized, depending on the peculiarities of the disease, the efficacy of treatment and the patient's tolerance to the drug.

Ordinarily adults are prescribed an initial dose of 0.1 g 2—3 times a day. When necessary the daily dose can be increased to 0.4—0.45 g.

Maximal doses for adults: single—3 tablets daily—8 tablets. Children are given the following doses: up to 5 years old 0.025 g twice a day, from 5 to 8 years 0.025 g 3—4 times a day, over 8 years, 0.1 g twice a day. When diphenylhydantoin sodium is not sufficiently effective, phenobarbital can be prescribed simultaneously.

If the patient has been receiving phenobarbital or other anticonvulsants before treatment with diphenylhydantoin is begun, it is recommended that the shift to the latter should be made by degrees, gradually reducing the dosage of

phenobarbital or other drugs and replacing them by increasing doses of diphenylhydantoin sodium

Treatment in combination with phenobarbital is usually carried out as follows: first week 0.05 g phenobarbital twice a day, and 0.05 g diphenylhydantoin sodium once a day; second week phenobarbital once a day, diphenylhydantoin sodium twice a day; third and succeeding weeks 0.05–0.1 g diphenylhydantoin sodium 3 times a day. The course of treatment is for 3–4 months.

It has been reported that diphenylhydantoin sodium is also effective in the treatment of paroxysmal tachycardia when the drug was taken in a dose of 0.1–0.15 g 3 times a day for 10–12 days; a reduction in the number and duration of attacks was observed.

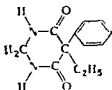
Various side effects may be observed during treatment with diphenylhydantoin sodium: vertigo, excitement, elevated temperature, difficult breathing, nausea, vomiting, tremor, ataxia, rash, hyperplasia of the gums, itching. When side effects are pronounced, the dose must gradually be lowered or the drug discontinued.

Diphenylhydantoin sodium is contraindicated in diseases of the liver and kidneys, decompensated cardiac activity and cardiac asthma.

To be stored in well stoppered bottles in a place protected from light, observing safety precautions (List B).

HEXAMIDIN (Hexamidineum)

4,6-Dioxo-5-ethyl-5-phenyl-hexahydropyrimidine



Synonyms: Desoxyphenobarbitone, Lepimidine, Lepsiral, Mylepsin, Myso-line, Primaclone, Primidone, Primidonum.

White or slightly yellowish crystalline powder (scaly platelets). Practically insoluble in water, ether and benzene; sparingly soluble in alcohol and acetone. Melting point 280–282°.

In its chemical structure, hexamidine is closely related to phenobarbital (the >CO group in position 2 is replaced by the >CH₂ group). It has an anticonvulsive action but unlike phenobarbital it has no marked hypnotic effect.

Used for treating epilepsy, chiefly in major convulsive attacks (grand mal). It is less effective in minor abortive attacks and psychic equivalents. In minor forms it usually has no constant influence but in some cases there is a sufficiently marked therapeutic effect.

Hexamidine is prescribed orally. Adults are usually given 0.125 g on the 1st and 2nd day of treatment (in the daytime or before retiring) and 0.25 g the 3rd day, the daily dose being then gradually increased by 0.25 g (every 3–7 days) until a total daily dose of 0.5–1.5 g is reached (0.25–0.5 g 2–3 times a day). The dose should be individualized, taking into account the effectiveness of the drug and the patient's tolerance.

Maximum doses for adults: single — 0.75 g, daily — 2 g.

Daily doses for children: from 3 to 6 years old 0.25–0.75 g, from 7 to 10 years 0.5–1 g, from 11 to 13 years 0.75–1.25 g, from 14 to 16 years 0.75–1.5 g.

If the patient has been receiving other anticonvulsants before the beginning of hexamidine treatment, hexamidine is prescribed in the doses stated and the daily dose of the other drugs is gradually reduced when the daily dose of hexamidine reaches 0.5–1 g; the other drugs are completely withdrawn. Treatment

with hexamidin must be lengthy (at least 6 months) The drug is withdrawn gradually

Hexamidin can be prescribed along with other anticonvulsants It is best administered with diphenylhydantoin sodium phenobarbital and bromides are less desirable because of the possible development of drowsiness

Hexamidin is only slightly toxic. During the first days of treatment side effects may be observed slight drowsiness vertigo headache ataxia and nausea anemia leukopenia and relative lymphocytosis may also develop These symptoms usually pass away of themselves

When necessary the dose is gradually reduced or the drug is completely withdrawn for several days after which it is given in a smaller dose When anemia develops it is recommended that folic acid (10—20 mg a day) and vitamin B₁₂ should be prescribed simultaneously with hexamidin

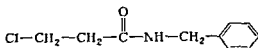
Hexamidin is contraindicated in diseases of the liver, kidneys and hematogenic system

Available in powder form and in tablets of 0.125 and 0.25 g

To be stored in well stoppered bottles in a place protected from light observing safety precautions (List B)

BENZYLCHLORPROPIONAMIDE (Benzylchlorpropionamidum)

N benzyl β chlorpropionamide



Synonyms Beclamidum, Benzchlorpropamide Chloracon Hibicon Nydrane Posédrine

White crystalline powder sparingly soluble in water (0.11%) freely soluble in alcohol Melting point 92.5—93.5°

Benzylchlorpropionamide has an anticonvulsive effect It is used in the treatment of epilepsy chiefly in major convulsive attacks and in psychomotor excitement It can also be prescribed for patients with abortive convulsive attacks The drug is particularly indicated for patients with heightened excitability and disordered attitude of mind It is prescribed orally the dosage for adults being 1 g 2—3 times a day If attacks continue the dose is increased to 4, 5 or 6 g daily Children are given doses of 0.25—0.5 g 2—4 times a day depending on the age frequency of attacks and the child's reaction to treatment Treatment is lengthy (up to 6 months or more)

If the patient has been receiving phenobarbital or other anticonvulsants they are withdrawn gradually it is recommended that administration of phenobarbital should be continued once a day (before retiring) since the complete withdrawal of the drug may cause major convulsive attacks The combined use of benzylchlorpropionamide and phenobarbital can also be recommended in this case the patient receives half a dose of benzylchlorpropionamide and 0.05 g phenobarbital in the morning benzylchlorpropionamide during the daytime and benzylchlorpropionamide plus phenobarbital before retiring

When treatment with benzylchlorpropionamide is successful and no attacks occur for a lengthy period of time the dose is gradually reduced the patient can be gradually shifted to treatment with phenobarbital (0.05—0.1 g before retiring or twice in 24 hrs) If attacks recommence benzylchlorpropionamide is again prescribed in the usual dosage.

During treatment with benzylchlorpropionamide watch must be kept over the function of the liver and kidneys as well as the blood picture

Available in powder form and tablets of 0.2, 0.25 and 0.5 g

To be stored in a dry place protected from light

TRIMETHINE (Trimethinum)
3,5,5-Trimethyloxazolidine 2,4-dione



Synonyms Absentol Edion Epidion Petidion, Plimal Tridione, Trimedol Trimethadionum Troxidon

White crystalline powder faint characteristic odour cooling bitter taste soluble in water freely soluble in alcohol ether and benzene Melting point 45—47°

Trimethine is used for the treatment of minor forms of epilepsy (petit mal) it is more effective for children It is also used in psychic and vascular autonomic equivalents It is not prescribed in major attacks

Trimethine is taken orally during or after meals The optimal dose is determined during the process of treatment Adults are usually prescribed 0.2—0.3 g 2—3 times a day children 0.1, 0.15 or 0.2 g 2—3 times a day

Maximal doses for adults single — 0.3 g daily — 0.9 g

Side effects may be observed during lengthy treatment or when there is heightened sensitivity to the drug photophobia rash and changes in the blood (neutropenia agranulocytosis anemia eosinophilia monocytosis) Treatment must be carried out under a physician's observation the blood must be examined at least every 10 days

Trimethine is contraindicated in cases of impaired function of the liver and kidneys and in diseases of the hematogenic organs and the optic nerve

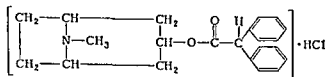
Available in powder form

To be stored in tightly closed glass containers in a dry place observing safety precautions (List B)

B Substances used for the treatment of parkinsonism

TROPACIN (Tropacinum)

Tropine diphenylacetate hydrochloride



White crystalline powder, feely soluble in water alcohol and chloroform partially insoluble in ether and benzene Melting point 212—216°

Tropacin is closely related to atropine in chemical structure and pharmacological properties (see p 97) but possesses a number of distinguishing characteristics Like atropine it lessens the excitability of the peripheral cholinergic systems and therefore causes a relaxation of the smooth muscles a diminution of secretion and dilation of the pupils In this respect however, it is less potent than atropine At the same time it is considerably more potent than atropine in its influence on the central cholinergic system (see p 87) Tropacin also has a pronounced ganglion blocking effect it inhibits the transmission of impulses in the ganglia of the autonomic division of the nervous

system and lessens their reactivity to chemical stimuli (acetylcholine, nicotine, cytosine)

Like papaverine, it also has a direct spasmolytic effect on the smooth muscles of the internal organs and blood vessels

Tropacin is mainly used in parkinsonism (after epidemic encephalitis and trauma, in manganese poisoning and other cases), Parkinson's disease, spastic paresis and paralysis (including infantile palsies) and other diseases accompanied by a heightening of the muscular tone. In the internal diseases clinic, it is prescribed in spasms of the smooth muscles of the abdominal organs, and in bronchial asthma and other conditions accompanied by a raising of the tone of the vagus and by spasms of the smooth musculature. In obstetrics, tropacin has proved to be an effective spasmolytic agent which inhibits uterine contractions; it can therefore be used when there is danger of premature labour and miscarriage.

Judging by experimental findings, tropacin is an effective agent for the treatment of poisoning with organo-phosphorous compounds.

Tropacin is usually administered orally in powders or tablets. The dose must be individualized, depending on the efficacy of treatment and the patient's tolerance.

The usual single dose for adults is 0.01–0.0125 g, which is prescribed once or twice a day. When there is good tolerance, the single dose may be increased to 0.015–0.02 g (in obstetric practice tropacin is prescribed in a dosage of 0.02 g twice a day). The daily dose is 0.025–0.05 g when there is good tolerance; this may be increased to 0.075 g.

The drug can also be administered orally in the form of a 1% solution (10–15 drops 2–3 times a day).

Maximal doses for adults: single — 0.03, daily — 0.1 g.

Single doses for children: up to 3 years old, 0.001–0.002 g; 3–5 years, 0.003–0.005 g; 6–9 years, 0.005–0.007 g; 10–12 years, 0.007–0.01 g.

The length of treatment depends on the character of the disease and its duration, and the effectiveness of treatment and tolerance for the drug. Treatment may be carried out for lengthy periods.

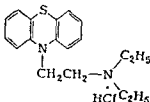
Tropacin is contraindicated in glaucoma. Due to its atropine-like action, dryness in the mouth and dilation of the pupils may be observed in some cases. These symptoms do not occur if the proper dosage has been selected; they are less pronounced than when digitalis preparations are used. In individuals with a heightened sensitivity to tropacin, the dose is reduced or the drug is given before retiring.

Available in powder form and in tablets of 0.01, 0.0125 and 0.015 g.

To be kept locked (List A) in well-closed bottles in a place protected from light.

DIETHAZINE (Diethazinum)

10 (2' Diethylaminoethyl)-phenothiazine hydrochloride



Synonyms: Antipar, Antiparkin, Casantin, Cosantin, Deparkin, Dinezine, Diparcol, Eazamine, Latibon, Parkazin, Thiantan.

White crystalline powder, freely soluble in water. Melting point 182–186°.

In its chemical structure, diethazine is closely related to chlorpromazine, promethazine and fenethazine; it is somewhat similar to them in pharmacological properties. Diethazine has moderate antihistaminic, peripheral cholinolytic

and ganglion blocking activity. It has a sedative effect and somewhat lowers the basal metabolism. It has a marked central cholinolytic action.

Used in treating parkinsonism. Parkinson's disease, torsional dystonia, etc.

Diethazine is prescribed orally in a dosage of 0.03–0.1 g 3–5 times a day, when there is good tolerance the daily dose is gradually increased to 1–1.2 g.

Diethazine is sometimes included as an ingredient of "Lytic mixtures" (see Chlorpromazine). Usually 5 ml of 0.5% solution is used for one injection.

Complications are possible when the drug is used: drowsiness, vertigo, adynamia and paresthesia. In rare cases erythematous rash is observed. When side effects are pronounced the dose is reduced or administration of the drug discontinued.

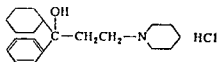
When working with diethazine care must be taken to prevent powder or solutions from coming into contact with the skin or mucous membrane.

Contraindicated in cases of impaired function of liver and kidneys, marked atherosclerosis and impaired cerebral circulation.

To be stored in hermetically closed containers of amber glass, observing safety precautions (List B).

CYCLODOL (Cyclodolum)

1-Phenyl-1-cyclohexyl-3-N-piperidylpropanol hydrochloride



Synonyms: Artane, Benzhexol hydrochloride, Paralest, Pargitan, Parkinson, Parkopan, Peragit, Pipanol, Trihexyphenidyl hydrochloride.

White crystalline substance, freely soluble in water. Melting point 243–245°.

Cyclochol has a strong central and peripheral cholinolytic effect. Used in parkinsonism, Parkinson's disease, Little's disease and spastic paralysis associated with lesions of the extrapyramidal system. In a number of cases, it lowers the tone and improves movements in paresis of a pyramidal character.

Prescribed orally in tablets, beginning with a dose of 0.001 g (1 mg) a day and then adding 1–2 mg a day until a daily dose of 0.003, 0.006 or 0.01 g (3, 6 or 10 mg) is reached. Doses must be individualized depending on effectiveness and tolerance. When using the drug, side effects associated with its cholinolytic properties may be observed: dryness in the mouth, impairment of accommodation, acceleration of pulse and vertigo. Side effects pass away when the dose is reduced or the drug withdrawn.

Available in tablets of 0.001, 0.002 and 0.005 g.

To be kept locked (List B).

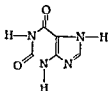
V AGENTS STIMULATING THE CENTRAL NERVOUS SYSTEM

a) Derivatives of purine

Purine is a compound containing two condensed heterocycles: pyrimidine (A) and imidazole (B).



Purine



2,6-Diethylxanthine (Xanthine)

Purine does not occur naturally in the free form but is obtained synthetically. Amino derivatives of purine, which are called purine bases (adenine, guanine) are constituents of nucleoproteins and are of great importance in the body's vital activities. The purine nucleus is also the basis of uric acid.

Some alkaloids of great importance as drugs are derivatives of 2,6-dioxypurine or xanthine; among them caffeine (1,3,7-trimethylxanthine), theobromine (3,7-dimethylxanthine) and theophylline (1,3-dimethylxanthine).

The principal pharmacological property of caffeine, the first representative of this group, is its stimulating influence on the central nervous system. For this reason it can be included in the group of so-called "analeptics" ("restorative" or "reviving agents").

Investigations carried out by I. P. Pavlov and his coworkers showed that caffeine heightens and regulates excitatory processes in the cerebral cortex; in the proper doses it intensifies positive conditioned reflexes and increases motor activity. Large doses may however lead to exhaustion of the nerve cells. The action of caffeine depends to a considerable degree on the type of higher neural activity; the dosage should therefore be set while taking into account the individual characteristics of neural activity.

Caffeine weakens the effect of hypnotics and narcotics.

The stimulating action of caffeine leads to a heightening of the capacity for mental and physical work and to a diminishing of fatigue and drowsiness.

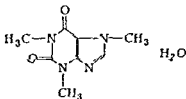
Caffeine increases the reflex excitability of the spinal cord and stimulates the respiratory and vasomotor centres. Cardiac activity is intensified under the influence of caffeine; contractions of the myocardium become more intense and the pulse is accelerated. In collapse and shock conditions the arterial pressure rises under the influence of caffeine; when arterial pressure is normal significant changes are not observed since simultaneously with the stimulation of the vasomotor centre and the heart the blood vessels of the striated muscles and other regions of the body are dilated (the vessels of the brain, heart and kidneys) the vessels of the abdominal organs (with the exception of the kidneys) are however contracted.

Uresis is somewhat increased under the influence of caffeine; this is mainly due to a diminution of reabsorption in the uriniferous tubules.

Theobromine and theophylline are similar in pharmacological action to caffeine but they have a considerably less stimulating influence on the central nervous system; at the same time they cause considerably greater dilation of the blood vessels and have a greater diuretic effect. Because of these characteristics theobromine and theophylline are discussed along with other vasodilators.

CAFFEINE (Coffeinum)

Trimethylxanthine or 1,3,7-trimethyl-2,6-dioxypurine



Synonyms: Guaranin, Guarin, Kaffein, Theinum.

Caffeine is an alkaloid contained in the leaves of tea (about 2%), the seeds of coffee (1–2%) and the nuts of cola. It is also obtained synthetically.

White, silky needles which effloresce in the air, odourless, bitterish, sparingly soluble in cold water (1:70), freely soluble in hot water (1:2), sparingly soluble in alcohol (1:50), very sparingly soluble in ether. Melting point 234–237°.

Solutions have a neutral reaction they are sterilized by holding at 100° for 30 min

Caffeine is used in depression of the central nervous system (as a stimulant increasing capacity for mental and physical work) in poisoning with narcotics insufficiency of the cardiovascular system and spasms of the vessels (migraine) Like other stimulants of the central nervous system caffeine is contraindicated in heightened excitability insomnia atherosclerosis organic diseases of the cardiovascular system and senility Caffeine is administered orally in powders or tablets Doses should be individualized the average dose for adults is 0.05—0.1 g 2—3 times a day

Maximal doses for adults single—0.3 g daily—1 g

Maximal doses for children 2 years old single—0.04 g daily—0.12 g 3—4 years single—0.05 g daily—0.15 g 5—6 years single—0.06 g daily—0.18 g 7—9 years single—0.075 g daily—0.25 g 10—14 years single—0.075—0.1 g daily—0.25—0.3 g Children up to 2 years old are not prescribed caffeine

Available in powder form and in combined tablets (Ascaphen Novomigrop hen Novocephalgin Pyramein Citramon see also Aspirin Aminopyrine)

To be stored in well stoppered bottles observing safety precautions (List B)
CAFFEINE SODIUM BENZOATE (Coffeinum natrio benzoicum Coffeinum et Natrii benzoas)

Double compound of caffeine and sodium benzoate

White powder odourless slightly bitter freely soluble in water (1:2) sparingly soluble in alcohol (1:40) Contains 38% caffeine Solutions are sterilized with running steam at 100° for 30 min

Similar to caffeine in pharmacological properties Indications and contraindications more soluble in water and more quickly excreted than pure caffeine

Administered subcutaneously in doses of 1 ml 10% or 20% solution and orally in powders and tablets (in doses of 0.1—0.2 g) In asphyxia neonatorum 0.1—0.25 ml of 10% solution is injected into the umbilical vein

Maximal doses for adults single—0.5 g daily—2 g

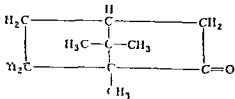
Maximal doses for children up to 6 months old single—0.05 g daily—0.15 g, from 6 months to 1 year single—0.05 g daily—0.15 g 2 years single—0.06 g daily—0.2 g 3—4 years single—0.08 g daily—0.25 g 5—6 years single—0.1 g daily—0.3 g 7—9 years single—0.15 g daily—0.5 g 10—14 years single—0.15—0.2 g daily—0.5—0.6 g

Available in powder form and in tablets of 0.1 and 0.2 g as well as in compound tablets (see Aspirin Aminopyrine Phenobarbital) Also available in ampoules containing 1 ml 10% or 20% solution or 2 ml 20% solution

To be stored in well stoppered bottles or sealed ampoules observing safety precautions (List B)

b) Drugs of the camphor pentylenetetrazol and nikethamide group

CAMPHOR (Camphora)



For medicinal purposes dextrorotatory natural camphor obtained from the camphor tree (Cinnamomum camphora) or from the camphor basil (Ocimum menthaefolium) is used as well as synthetic levorotatory camphor produced from pine oil

561
White crystalline lumps or colourless crystalline powder, characteristic odour, spicy, bitter and then "cooling" taste, very sparingly soluble in water (1 : 840), freely soluble in alcohol, ether, chloroform and fatty and volatile oils. To be stored in well closed containers in a cool place. Camphor is incompatible with salol, menthol and chloralhydrate (liquefies)

When applied locally, camphor preparations have an irritating and to some extent, an antiseptic action. They are accordingly used in the form of ointments and liniments in inflammatory processes, rheumatism, etc.

When absorbed, camphor excites the central nervous system and stimulates respiration and the circulation. The stimulation of respiration and increased volume of the pulse which ensue when solutions of camphor in oil are injected subcutaneously are partly due to the local irritation and resulting reflex influence on the respiratory and vasomotor centres and on the heart. Camphor also has a direct influence on the myocardium, increasing metabolic processes and heightening its sensitivity to the sympathetic nerve (A. S. Saratkov)

Camphor is administered subcutaneously (in the form of oil solutions) and orally in acute and chronic cardiac weakness and collapse, it is also used to stimulate respiration and the circulation in croupous pneumonia and other infectious diseases and in poisoning with narcotics and hypnotics, etc.

It is sometimes used in large doses for the convulsive therapy of schizophrenia

The following preparations of camphor are employed

Camphorated oil, 20%, in ampoules A 20% solution of camphor in ampoules (Solutio camphorae oleosa 20% in ampullis, Oleum camphoratum 20% in ampullis) A 20% solution of camphor in persic oil, oily liquid of light yellow colour and odour of camphor. Specific gravity 0.925—0.928

Administered subcutaneously in the following doses adults, 1 2 or 5 ml children up to 1 year old 0.5—1 ml from 2 to 5 years 1—2 ml from 6 to 12 years, 1—3 ml

Powdered camphor (Camphora trita) Obtained by grinding camphor with a small amount of alcohol or ether

Usually administered orally in doses of 0.1—0.2 g Children are prescribed from 0.01 to 0.075 g depending on the age

Camphorated oil for local application (Oleum camphoratum ad usum externum) A 10% solution of camphor in sunflower oil. Transparent oily liquid of yellow colour and strong odour of camphor. Specific gravity 0.924—0.928

Applied locally by rubbing in. To be stored in well stoppered bottles in a cool place, protected from light

Camphor ointment (Unguentum camphoratum) Composition powdered camphor 1 part, petrolatum 6 parts, lanolin 3 parts. Homogeneous yellow ointment with odour of camphor. Applied locally by rubbing in (in muscular pain rheumatism, sciatica, etc)

Spirit of camphor (Spiritus camphoratus) Composition camphor 1 part, alcohol 7 parts, water 2 parts

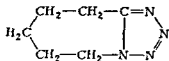
Transparent colourless liquid with odour of camphor. Applied locally by rubbing in

To be stored in well stoppered bottles

Bromated camphor (see p. 22)

PENTYLENETETRAZOL (Pentylene-tetrazolum)

Pentamethylenetetrazol



Synonyms Angiazol, Cardiazol, Centrazol, Corazol, Deumacard, Diovascol, Leptazol, Metrazol, Pentamethazolum, Pentazol, Pentetrazolum, Pentrazol, Pentylene-tetrazol, Phrenazole, Stellacardiol, Tetracor, Vasazol

White crystalline powder, freely soluble in water and alcohol Melting point 59—61° Aqueous solutions have a neutral reaction Solutions are sterilized by holding at 100° for 30 min

In its pharmacological properties pentylenetetrazol is similar to camphor, caffeine and nikethamide

An advantage of pentylenetetrazol over camphor is its good solubility in water and lipids, this promotes its rapid absorption by the subcutaneous tissue and the mucosa of the gastrointestinal tract Because of its free solubility in water the drug can be administered intravenously

Pentylenetetrazol is excreted more rapidly than camphor, and its effect is of shorter duration

Pentylenetetrazol has a stimulating influence on the central nervous system it stimulates respiration and the circulation and in large doses causes convulsions

Used to stimulate the cardiovascular system and respiration and as an agent promoting the ending or weakening of anesthesia it is also used for the so called "convulsive therapy of schizophrenia"

The dosage and method of administration depend on the indications In shock asphyxia decline in cardiac activity during operations etc. the slow intravenous injection of 1 ml 10% solution is recommended followed by the subcutaneous or intramuscular administration of 1—2 ml of the same solution when necessary

In cases of poisoning with narcotics hypnotics and morphine or other analgetics 2—3 ml 10% solution is infused into the vein simultaneously administering the same amount intramuscularly

In infectious diseases and chronic cardiac weakness pentylenetetrazol is prescribed orally in a dosage of 0.1 g 2—3 times a day If necessary injections of 1 ml 10% solution are given subcutaneously

Doses for children up to 1 year old 0.015—0.02 g orally (powder or solution) or 0.15—0.2 ml 10% solution subcutaneously from 2 to 5 years 0.03—0.05 g orally or 0.3—0.5 ml 10% solution subcutaneously from 6 to 12 years 0.06—0.08 g orally or 0.6—0.8 ml 10% solution subcutaneously

In obstetric practice pentylenetetrazol is administered to women in labour when there is danger of asphyxiation of the foetus in a dose of 1 ml 10% solution intravenously or intramuscularly

In all cases when pentylenetetrazol is used for medical purposes intravenous administration must be performed slowly (1 ml in 1—2 min) Rapid administration may lead to convulsions

Maximal doses for adults (orally and subcutaneously) single—0.2 g daily—0.5 g

Maximal doses for children up to 6 months old single—0.02 g daily—0.04 g from 6 months to 1 year single—0.02 g daily—0.06 g 2 years single—0.03 g daily—0.09 g 3—4 years single—0.05 g, daily—0.15 g 5—6 years single—0.06 g daily—0.2 g 7—9 years single—0.075 g daily—0.2 g 10—14 years single—0.08 g daily—0.25 g

In order to cause convulsive attacks in the treatment of schizophrenia 3—5 ml 10% pentylenetetrazol solution is injected rapidly into the vein through a needle of large diameter (1 ml per sec) The convulsive attack comes on either during the injection or 15—20 sec later A total of 10 attacks are induced with an interval of 2 days between each attack (i.e. each 3rd day) If an attack does not develop from the dose indicated the dose for the next injection is increased by 0.5—1 ml of the same solution When carrying out convulsive therapy measures must be taken to prevent traumatic injury to the patient

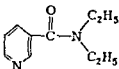
Contraindications for the use of pentylenetetrazol serious affections of the heart pulmonary diseases especially tuberculosis in an active form, acute febrile conditions predisposition to convulsive reactions

Available in powder form, in tablets of 0.1 g and in ampoules containing 1 ml 10% solution

To be stored in well stoppered bottles or sealed ampoules, observing safety precautions (List B)

NIKETHAMIDE (Nikethamidum)

25% solution of the diethylamide of nicotinic acid



Synonyms Anacardon, Cardiamidum, Coraethamidum Coramin, Cordiamin, Cordiol, Cormed, Corvitol, Corviton, Dinacoryl, Eucoran, Nicethamidum, Nickamide, Nicorine, Nikorin, Pyricardul, Stiminol, Tonocard

Colourless or yellowish liquid, characteristic odour, miscible with water and alcohol in all proportions. Specific weight 1.023—1.024

Stimulates the central nervous system and respiration and tonizes the cardiovascular system. In the character of its action, nikethamide is similar to camphor, caffeine and pentylenetetrazol, particularly the latter. Nikethamide is freely soluble in water and is easily absorbed by the subcutaneous tissue, muscles and mucous membranes, it can be administered subcutaneously, intramuscularly and intravenously, as well as orally.

Used in acute and chronic impairment of cardiac activity, cardiac weakness and weakened respiration in infectious diseases and during convalescence in acute collapse and asphyxia, in poisoning with narcotics and hypnotics (particularly barbiturates), morphine, carbon monoxide, hydrocyanic, etc., in shock conditions, collapse and asphyxia during surgical operations and the postoperative period, as well as in serious infectious diseases, in asphyxia neonatorum.

Prescribed subcutaneously, intramuscularly and intravenously. Doses for adults, 1 ml 1—2 times a day, doses for children, from 0.1 to 0.75 ml depending on the age. In cases of poisoning with narcotics, hypnotics and analgetics, large doses are given (for adults 2—3 ml). Intravenous administration must be performed slowly. Orally, adults are given 20—25 drops 2—3 times a day, children are given one drop for each year of their age.

Maximal doses for adults orally, single dose—1 ml (30 drops) daily—3 ml (90 drops), subcutaneously, single—1 ml, daily—3 ml, subcutaneously and intravenously in cases of poisoning with narcotics—3 ml (single injection).

Maximal doses for children up to 6 months old single dose orally—2 drops, subcutaneously—0.1 ml, daily dose orally—4 drops, subcutaneously—0.2 ml, from 6 months to 1 year, single dose orally—3 drops, subcutaneously—0.1 ml, daily dose orally—6 drops, subcutaneously—0.2 ml, 2 years, single dose orally—4 drops, subcutaneously—0.15 ml, daily dose orally—8 drops, subcutaneously—0.3 ml, 3—4 years, single dose orally—5 drops, subcutaneously—0.25 ml, daily dose orally—15 drops, subcutaneously—0.5 ml, 5—6 years, single dose orally—6 drops, subcutaneously—0.5 ml, daily dose orally—18 drops, subcutaneously—1 ml, 7—9 years, single dose orally—7—8 drops, subcutaneously 0.5 ml, daily dose orally—20—25 drops, subcutaneously—1 ml, 10—14 years, single dose orally—10—14 drops subcutaneously—0.8 ml, daily dose orally—30 drops, subcutaneously—1.5 ml.

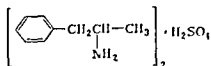
Available in ampoules of 1 and 2 ml for injections, and in vials of 10 and 30 ml for oral administration.

Safety measures must be observed in storage (List B). The solution for oral administration is kept in vials of amber glass with ground glass stoppers, the solution for injections is kept in sealed ampoules in a place protected from light.

c) Drugs of the phenamine group (phenylalkylamines)

PHENAMINE (Phenaminum)

d, 1 β Phenylisopropylamine (or 1 phenyl-2 aminopropane) sulfate



Synonyms Amphetamin sulfas, Amphetaminum, Benzedrin sulfate Benzpropamine, Dopamine, Elastonon, Euphobine, Euphodine, Isamin Mecodrin Orthedrin Phenedrin Psychedrinum Psychoton, Racephen, Rapietamine, Sympamin, Zedrine (Actedron is the corresponding phosphate)

White, fine crystalline powder, bitter taste, soluble in water (1 : 20 in cold water and 1 : 3 in hot) very sparingly soluble in alcohol, practically insoluble in ether

Phenamine is a potent analeptic, it differs from other substances of this group in that its stimulating effect on the central nervous system is combined with an active influence on the sympathetic division of the nervous system

In its chemical structure and pharmacological properties, phenamine is closely related to the drugs of the adrenalin group. Its chief difference from adrenalin, chemically, is the absence of hydroxyls in the aromatic cycle and the aliphatic chain, this gives it greater stability and prevents it from being broken down in the liver, the branched aliphatic chain preserves the molecule from oxidizing desamidization by aminoxidase, an enzyme which breaks down adrenalin and closely related amines

Thanks to its stability in the body the effects of phenamine are of very long duration and are manifested when the drug is taken orally

Phenamine's similarity to adrenalin determines its adrenomimetic action. It induces contraction of the peripheral vessels, intensification of the contractions of the heart, raising of arterial pressure, relaxation of the muscles of the bronchi and dilation of the pupils. Phenamine heightens the excitability of the respiratory centre and causes an intensification and acceleration of respiration

When the correct dosage is used phenamine intensifies excitatory processes, diminishes a feeling of fatigue and has a general stimulating influence which is manifested in a sensation of fresh energy, briskness, increased capacity for work and less need for sleep. It has a wakening effect in sleep induced by hypnotics and narcotics

When phenamine is used a lessening of the appetite is observed, and a feeling of satiation comes on more quickly

The effect of phenamine, like that of other analeptics depends on the condition of neural activity. Doses should be individualized, large doses may cause exhaustion of the nerve cells

In a number of cases (10—15%) there are reactions of an opposite character ("paradoxical reactions") when phenamine is used: apathy instead of excitement and lowered capacity for work. For that reason it is absolutely essential that before prescribing phenamine a test should be made for tolerance, i.e., the reaction after a single administration should be observed

According to contemporary conceptions, the mechanism of phenamine's adrenomimetic action lies in its ability to reduce the activity of aminoxidase and in this way stabilize adrenalin and noradrenalin formed at the endings of the adrenergic nerves. In this respect it is similar to ephedrine. There are grounds for considering that the stimulating effect of phenamine on the central nervous system is also partly to be explained as being due to the inhibition of aminoxidase. It should be noted that under the influence of aminoxidase, aldehydes are for

med which inhibit oxidizing processes. It is not to be excluded that by reducing the activity of aminoxidase phenamine promotes a limitation of the formation of aldehydes and an improvement of metabolic processes in the nerve tissue.

Phenamine is chiefly used in psychoneurological practice for the treatment of psychogenic depression, narcolepsy, the sequelae of encephalitis, alcoholic depressive psychosis and other diseases accompanied by drowsiness, lassitude, apathy and asthenia. It has been reported that phenamine is effective in postencephalitic parkinsonism (in combination with cholinolytic drugs). It is also used in cases of poisoning with narcotics and hypnotics.

As a stimulant of the central nervous system, phenamine is used to overcome fatigue and temporarily raise the capacity for physical and mental work. It must, however, be borne in mind that the lengthy use of phenamine for this purpose is impermissible since it only mobilizes the body's reserves and does not obviate the need for normal rest and the recuperation of strength.

Due to its vasoconstrictive effect, phenamine is sometimes employed as an antiphlogistic in rhinitis and sinusitis (see Ingaphen).

Phenamine is prescribed orally for adults in a dosage of 0.005–0.01 g once or twice a day. The effect from a single dose lasts 2–8 hours. In psychiatry, phenamine is sometimes given in courses of 10–12 days. At times it is prescribed along with phenobarbital in the treatment of epilepsy (to lessen drowsiness). The drug is not prescribed for small children; when necessary it is given to children 7 years old in a dose of 0.0015 g. For children 8–14 years old, the dosage is 0.002–0.005 g.

Phenamine has recently been proposed for treating uterine inertia during labour (a single dose of 20 mg orally). Administration of the drug diminishes the patient's fatigue and induces an intensification of the birth process. Phenamine should not be used in late toxemia of pregnancy with a hypertensive syndrome.

Maximal doses for adults: single — 0.01 g daily — 0.02 g. For stimulating labour, a single dose of 0.02 g is permissible. In the prescription, the dose must be written out in words followed by an exclamation mark.

Phenamine must be used with care. Overdosage leads to nausea, chills, vertigo, insomnia, loss of appetite, tachycardia and at times impairment of cardiac activity (arrhythmia). The drug is excreted slowly and cumulative symptoms and the development of habituation are possible.

Contraindications for the use of phenamine: senility, insomnia, state of excitement, diseases of the liver, hypertension, atherosclerosis and organic diseases of the cardiovascular system.

Available in powder form and in tablets of 0.01 g.

To be kept locked (List A) in well stoppered bottles. To be dispensed with the same restrictions as narcotics.

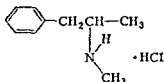
Ingaphen. A pocket inhaler containing a piece of cloth impregnated with a mixture of phenamine, menthol, eucalyptus oil and lavender oil.

Used in rhinitis and sinusitis, the phenamine contained in the inhaler promotes the contraction of the vessels of the mucous membrane of the nose and diminishes inflammatory manifestations (see also Ingacamph).

In order to avoid insomnia, the inhaler should not be used in the evening or before retiring.

DESOXYEPHEDRIN (Desoxyephedrinum)

d, 1 β Phenylmethylisopropylamine hydrochloride (or 1-phenyl-2-methylaminopropane)



Synonyms Adipex Amphedroxyn Defroxin Desamin Desoxyn Desoxyphed Desoxyphed Dexophrine, Dexoval Dextim Doryfed Drinalfa Effro xine Estimulex Euphadrinal Gerobit Isophan Methamphetamine, Methamphin Methedrin Metloxyn Methylbenzedrin Methylisomin Neodrine Norodrin Per vinlin Philopon Premodrin Semoxydrine Syndrox, Tonedron

White crystalline powder bitter taste soluble in water

Desoxyephedrin is closely related to phenamine in chemical structure and pharmacological properties. It is more potent than phenamine but also more toxic.

Used as a stimulant of the central nervous system in physical and mental fatigue and in depressive states can also be used to stimulate labour.

Prescribed orally 1 tablet (0.003 g) once or twice a day

Contraindications are the same as for phenamine

Habituation is also possible with desoxyephedrin

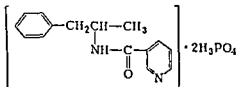
Available in tablets of 0.003 g (3 mg)

To be kept locked (List A) in a place protected from light

To be dispensed with the same restrictions as phenamine

PHENATINE (Phenatimum)

Diphosphate of β phenylisopropylamide of nicotinic acid condensation product of phenamine and nicotinic acid



Colourless crystals or white crystalline powder odourless salt bitter taste freely soluble in water soluble in alcohol practically insoluble in ether Melting point 162—166° Solutions withstand sterilization by the usual methods and are stable in storage pH of 5% solution 1.8—2.4

Phenatine has a stimulating effect on the central nervous system in which respect it is similar to phenamine. It is distinguished from phenamine by having a "milder" action and also by the fact that it does not cause a contraction of the blood vessels or raise the arterial pressure—on the contrary the arterial pressure falls under the influence of phenatine this makes it possible to prescribe phenatine when necessary as a stimulant of the central nervous system in patients with hypertension.

Indications for the use of phenatine are the same as for phenamine. It has also been proposed that phenatine should be used as a hypotensive. It has been reported that phenatine can be used successfully in the treatment of obesity.

Prescribed orally in a dosage of 0.05—0.15 g 2—3 times a day the first two or three days and then 3 times a day Subcutaneously 1 ml 5% solution is injected once or twice a day the course of treatment is 20—40 injections

Maximal doses for adults single—0.2 g daily—0.6 g

In isolated cases use of phenatine leads to headache and pain in the region of the heart At times dermal pruritus develops in such cases 1 tablespoonful of 10% calcium chloride solution is given orally 3 times a day

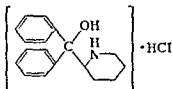
Available in powder form and in tablets of 0.05 g

To be kept locked (List A) in tightly stoppered bottles Conditions to be observed in dispensing are the same as for phenamine

d) Derivatives of diphenylmethane

PIRIDROL (Piridrolum)

α (2 piperidyl) benzohydrochloride



Synonyms Gerodyl, Leptidrol Luxidin, Meratran, Merefran, Pipradol
Pipradol, Pipral

White crystalline powder, freely soluble in water Melting point 286—288°

Piridrol is a stimulant of the central nervous system it has an exciting action diminishing the hypnotic effect of barbiturates and the sedative effect of neuroplegic substances, as well as increasing motor activity In its influence on the central nervous system, piridrol is similar to phenamine Unlike phenamine it does not influence the peripheral adrenoreactive systems it does not cause a contraction of the blood vessels an elevation of the arterial pressure, etc

Piridrol is used in psychiatric practice and in the nervous diseases clinic as an agent stimulating the central nervous system in asthenia, depressive states, narcolepsy sluggish schizophrenia, etc The drug is also effective in the "neuroleptic" syndrome caused by the use of chlorpromazine, reserpine and other neuroplegic drugs

Piridrol is prescribed orally in tablets in a dosage of 1 mg 2—3 times a day, if the effect is insufficient and the drug is tolerated well, the dose can be increased to 2.5 mg 3 times a day In order to avoid disturbed sleep at night piridrol should not be administered in the afternoon The course of treatment can continue 2—4 weeks or more

When piridrol is used, uneasiness motor excitement and tachycardia may be observed In such cases the dose should be reduced When administered over a lengthy period the development of tolerance and habituation is possible

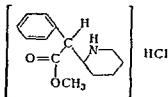
Piridrol is contraindicated in insomnia, atherosclerosis hyperthyposis, pronounced emaciation and psychic excitement.

Available in powder form and in tablets of 0.001 and 0.0025 g (1 and 2.5 mg)

To be kept locked (List A) in tightly closed containers

MERIDIL (Meridilum)

Methyl phenyl (2) piperidylacetate hydrochloride



Synonyms Centedrin, Methylphenidate hydrochloride, Ritalin

Meridil is a stimulant of the central nervous system In its pharmacological properties it is closely related to piridrol but its stimulating effect is milder, it has no influence on the peripheral adrenoreactive systems

Used in psychiatry and the nervous diseases clinic in depressive states, including climacteric and senile psychoses also used to diminish the depression

caused by reserpine chlorpromazine and other neuroplegic drugs etc Administered orally in a dosage of 0.01—0.015 g (10—15 mg) 2—3 times a day The course of treatment ranges from 2—4 weeks to 3—4 months

Meridil is usually tolerated well In isolated cases heightened irritability uneasiness and insomnia may be observed

Safety precautions must be observed in storage (List B)

e) Hydrazines

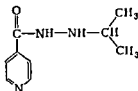
During recent years it was discovered that a number of compounds containing the hydrazine group have a stimulating effect on the central nervous system This was first established when using 2 isopropyl 1 isonicotinoylhydrazine as an antituberculosis agent This compound is closely related to the hydrazine of isonicotinic acid in structure and chemotherapeutic activity (see Isoniazid) Along with its therapeutic antituberculosis effect 2 isopropyl 1 isonicotinoylhydrazine caused symptoms of stimulation of the central nervous system euphoria heightened reflex excitability insomnia and at times psychotic reactions It was subsequently demonstrated that other analogous compounds have a still greater stimulating effect on the central nervous system Investigations into the mode of action of these substances established the fact that they have the ability of strongly inhibiting the activity of monoaminoxidase — an enzyme involved in the inactivation of 5 hydroxytryptamine (serotonin), noradrenalin and other biogenic amines After the administration of these hydrazines there is an increase in the content of biogenic amines in the central nervous system and other organs and tissues According to present day conceptions noradrenalin and serotonin play an important role in regulating the functions of the central nervous system The possibility therefore that the stimulating effect of 2 isopropyl 1 isonicotinoylhydrazine and its analogues is to a certain extent associated with their antiaminoxidase activity is not to be ruled out It should be noted that these compounds are antagonists of reserpine (see p 31) and lessen its sedative hypothermic and other effects

In medical practice these substances have proved effective in the treatment of depressive states in psychic patients

Of this group of drugs the Pharmacological Committee of the USSR Medical Academy and the Health Ministry has approved Iprazid for use in medicine

IPRAZID (Iprazidum)

2 Isopropyl 1 isonicotinoylhydrazine



Synonyms Iproniazid Ipronid Marsalid Marsilid

White crystalline powder freely soluble in water Melting point 112—114°

Iprazid has diversified pharmacological activity It inhibits monoaminoxidase in vitro and in vivo weakens the effects caused by reserpine prolongs the action of barbiturates (amobarbital sodium hexobarbital sodium etc), intensifies the hypothermic and sedative effects of chlorpromazine and other phenothiazine derivatives lowers the arterial pressure and has a weak cholinolytic and adrenergic effect The drug is cumulative in its action the toxicity increases with repeated administration

Iprazid is used in psychiatry in treating patients in a mild or moderate depressive state in mildly manifested depression in patients with a circular

psychosis in slight involutional depression in schizophrenic patients with a predominantly depressive syndrome, etc. Iprazid can be administered along with reserpine in order to lessen the symptoms of depression caused by the latter. Caution must be observed when iprazid is used in combination with chlorpromazine, since along with an intensification of the effect from the latter there may also be an increase in its toxicity.

According to information in the literature iprazid abolishes the pain in patients with angina pectoris. It is possible that this effect is also associated with the inhibition of monoaminoxidase and a change in the metabolism of the pyrocatechinamines (noradrenalin and adrenalin) in the muscle of the heart.

Iprazid is prescribed orally in tablets or dragees in a dosage of 0.025–0.05 g 3–4 times a day. In mild depression smaller doses can be used (0.01–0.025 g per day). The drug's action develops slowly but the effect remains for a lengthy period after it is withdrawn. Usually an improvement in the patient's condition sets in within 1–2 weeks, the dose is then gradually reduced to 0.05–0.1 g a day. The course of treatment continues 6–8 weeks after which the drug is prescribed in small "maintenance" doses (0.01–0.025 g per day). It is recommended that iprazid should be taken in the morning.

Side effects may be observed when iprazid is used: vertigo, irritableness, insomnia, paresthesia, constipation, retention of the urine, impaired accommodation, anemia and icterus. A fall in the arterial pressure and orthostatic collapse is possible. In some patients a hypomanic condition may develop. For that reason treatment with iprazid must be carried out under the careful observation of a physician; the blood picture and the function of the liver and kidneys must be checked periodically, and the arterial pressure measured. Side effects usually pass away when the dose is reduced, when necessary, administration of the drug is discontinued. It is recommended that vitamin B₆ should be given during treatment.

Contraindications for the use of iprazid: deep depression, epilepsy, psychic excitement, insufficiency of the liver and kidneys, pronounced atherosclerosis, pronounced cardiac insufficiency, anemia.

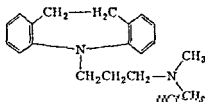
Available in powder form and in tablets of 0.01, 0.025 and 0.05 g.

To be stored in a cool, dry place, observing safety precautions (List B).

1) Derivatives of iminodibenzyl

IMIZIN (Imizinum)

N (γ dimethylaminopropyl) iminodibenzyl hydrochloride



Synonyms: Imipramine, Tofranil

White crystalline powder, freely soluble in water. Melting point 170–174°
pH of 1% solution 6.5

In its chemical structure imizin is related to promazine and chlorpromazine (see pp 28–25) although the structure of the ring system is different. Unlike promazine and chlorpromazine imizin has no marked neuroleptic effect; it is only in relatively large doses that it has a mild sedative effect, relaxing the skeletal muscles and somewhat lowering the body temperature, it has a moderate cholinergic and adrenergic effect.

In psychiatric practice imizin has proved to be an effective agent in treating depressive conditions of diverse etiology especially in cases of a manic depressive syndrome accompanied by motor and ideation inhibition diurnal fluctuations in mood and mildly manifested delirious ideas. The administration of imizin improves the general condition and causes a general calming, an abatement of internal strain and an improvement in the mood.

Because of the peculiarities of the therapeutic effect of imizin and drugs of this type it has been proposed that they be termed "thymoleptic" or "euthymic substances" (Kilholz and Battegay, Facio et al.)

Imizin is administered intramuscularly and per os. Treatment is usually commenced with the intramuscular administration of 0.025 g (25 mg) 2—4 times a day (injected into the gluteus maximus) after several days the dose is gradually increased 0.025 g a day up to 0.05 g 3—4 times a day in 10—14 days reduction of the dose for injections is commenced the drug being simultaneously prescribed orally each 25 mg for injection is replaced by 50 mg in the form of a dragée. The daily dose of the drug amounts to 0.25—0.3 g (250—300 mg). When a therapeutic effect has been achieved the dose is gradually lowered 0.025 g per day.

Imizin can also be prescribed only orally. Treatment is begun with a dose of 0.075—0.1 g a day gradually increasing this to 0.25—0.3 g a day then the dose is reduced. It is also possible to begin with higher doses (0.15—0.2 g a day) gradually reducing the dose as a therapeutic effect sets in.

Doses of imizin and the length of treatment are individualized depending on the character of the disease, the patient's condition, the effectiveness of treatment and tolerance for the drug. Ordinarily the course of treatment is for 1½—2 months after which the administration of maintenance doses is begun on an out-patient basis (0.025 g orally 2—6 times a day). If treatment is stopped too soon this may lead to a fresh onset of depression.

Imizin is usually tolerated well. In isolated cases there may be dryness in the mouth, sudoresis, vertigo, palpitation, impairment of accommodation and muscular weakness. In such cases the dose is reduced.

The drug should not be prescribed for excited patients. Because of its irritating effect caution must be observed in prescribing it orally for psychic patients suffering from ulcer of the stomach.

When administering imizin parenterally it must be borne in mind that solutions of the drug may have an irritating effect on the tissues.

Available in ampoules containing 2 ml of 1.25% solution (25 mg in 1 ampoule) and in dragees of 25 mg.

To be stored in a dry place protected from light observing safety precautions (List B). When working with the drug measures must be taken to prevent it coming into contact with the skin and mucous membranes.

g) Plant extracts and animal tissue preparations which have a stimulating effect on the central nervous system

SCHIZANDRA FRUIT AND SEEDS (Fructus et semina Schizandrae chinensis Baill.)

The dried fruit and seeds of a climbing shrub or vine of the family Magnoliaceae widespread in Primorsk and Khabarovsk Territories.

Contains a crystalline substance, schizandrin, as well as volatile oil, organic acids, carbohydrates, vitamin C and other substances. Has a stimulating effect on the central nervous system, intensifies positive conditioned reflexes and stimulates the cardiovascular system and respiration. Increases the capacity for work in conditions of mental and physical fatigue.

Used as a stimulant of the central nervous system in conditions of physical strain, physical and mental fatigue, excessive drowsiness, etc.

Administered orally in the form of a tincture or in powders and tablets. The preparation is taken on an empty stomach or 4 hours after meals. The effect

sels in within 30—40 min and lasts 4—6 hours after a single dose. *Schizandra* tincture is made with 96° alcohol. 20—30 drops are given twice a day. It has been reported that a fluid extract of *Schizandra* seeds made with 70° alcohol (1:3) is effective in stimulating labour. For this purpose a dose of 20—25 drops of the extract is given 3 times at intervals of an hour.

Schizandra like other stimulants should only be taken on a physician's prescription and under his observation in order to avoid over stimulation of the nervous and cardiovascular systems.

Schizandra preparations are contraindicated in nervous excitement, insomnia, elevated arterial pressure and impairment of cardiac activity.

GINSENG ROOT (*Radix Ginsengi*)

The root of a perennial herb *Panax schinseng* Nees & V. Esenb. (syn *Panax ginseng* C. A. Mey.) of the family *Araliaceae* found in the eastern part of the USSR, south east China and Korea. The roots of the five leaved ginseng (*Panax quinquefolium*), widespread in North America and of the creeping ginseng (*Panax repens*) found in Japan are also used in medical practice. All these species are cultivated. Roots of 5—6 year old plants gathered in the autumn are used.

Ginseng root contains volatile and fatty oil, pectins and other carbohydrates, glycosides (panaxosides A and B, panaxilon, panaxin), saponins and other substances, alkaloids have not been found. The chemical nature and pharmacological properties of the substances contained in ginseng have as yet not been studied sufficiently.

Preparations of ginseng root are used as tonics in hypotonia, fatigue, over strain and neurasthenia.

Administered orally (before meals) in the form of a 10% tincture (15—25 drops 3 times a day) or powders (0.25—0.3 g).

Rp T rac Ginsengi 200

DS 15—20 drops 3 times a day

LEUZEA — rootstock and root (*Radix Leuzeae carthamoidis*). The cleaned rootstock and roots of the herb *Leuzea carthamoides* DC. (syn *Rhaponticum carthamoides*) — of the family *Compositae*. It grows in the mountains of the Altai Territory in western and eastern Siberia and in Middle Asia.

Contains inulin, volatile oils, resins, salts of organic acids and other substances.

Leuzea preparations have been proposed as agents stimulating the central nervous system and increasing capacity for work in conditions of mental and physical fatigue.

The chemical composition and pharmacological properties of *Leuzea* are still being studied.

Available in the form of a tincture and a fluid extract made with 70° alcohol (*Extractum Leuzeae carthamoidis fluidum*). Tincture and extract are prescribed in a dosage of 20—30 drops 2—3 times a day. Should be used on the instructions of a physician and under his observation.

The length of treatment is 2—3 weeks or more depending on indications.

Rp T rac Leuzeae carthamoidis 200

DS 20—30 drops twice a day (before meals)

Rp Extr Leuzeae carthamoidis fluidi 200

DS 20—30 drops 3 times a day (before meals)

Echinopanax tincture (*Tinctura rhizomatis et radices Echinopanacis elati*)

Tincture (made with 70° alcohol) of the roots of *Echinopanax elatum* family *Araliaceae*, a shrub found in the Far East. The roots contain saponins, traces of alkaloids and glycosides and volatile oil.

The tincture is a transparent light brown liquid with a bitter taste and a characteristic odour.

In its physiological effect echinopanax tincture is similar to ginseng. It is used as an agent stimulating the central nervous system in asthenic and depressive states and in hypotonia.

Administered orally in a dosage of 30—40 drops 2—3 times a day, before meals.

Rp T rac Echinopanacis elati 250

DS 30—40 drops 2—3 times a day

STERCULIA TINCTURE (Tinctura foliorum Sterculiae platanifoliae)

A 20% tincture (made with 70° alcohol) of the leaves of *Sterculia platanifolia* family Sterculiaceae a tree which grows in the Crimea and the Caucasus along the shore of the Black Sea.

Transparent greenish brown liquid of bitterish taste.

Used as a stimulant in asthenic and depressive conditions, overstrain and hypotonia.

Prescribed orally in a dosage of 10—40 drops 2—3 times a day. Course of treatment 3—4 weeks. If side effects appear such as dryness in the mouth, palpitation, heightened irritability or deterioration of sleep, the dose is reduced and a break made in treatment. The tincture should not be taken in the evening, especially before retiring.

Available in vials containing 50 ml.

To be stored in a cool place protected from light.

Rp Tincturae Sterculiae 500

DS 15—20 drops 2—3 times a day

ARALIA TINCTURE (Tinctura Araliae)

A 20% tincture (made with 70° alcohol) of the roots of Manchurian aralia (*Aralia Manchurica* Rupr et Maxim) of the family Araliaceae.

Transparent amber coloured liquid characteristic odour, spicy taste. Contains traces of alkaloids, volatile oil, saponins, glycosides.

The tincture has a stimulating effect on the central nervous system. Used in hypotony, asthenia and depressive conditions. Prescribed orally in a dosage of 30—40 drops 2—3 times a day.

Contraindicated in cases of heightened nervous excitability, insomnia or hypertensive disease. To be dispensed only on a physician's prescription.

PANTOCRIN (Pantocrinum)

Fluid alcoholic extract of the unossified antlers (panti) of the Siberian Stag (Maral), Manchurian Deer (Isubr) and Spotted Deer. Transparent, slightly yellowish liquid.

Used as a tonic in overstrain, neurasthenia, neurosis, asthenic conditions after acute infectious diseases, myocardial weakness, hypotonia.

It has been reported that pantocrin raises the coagulability of the blood in patients with hemophilia; these findings, however, must be further verified.

Pantocrin is administered orally, subcutaneously or intramuscularly.

The dosage for oral administration is 30—40 drops 2—3 times a day; dosage for injections — 1—2 ml daily. Course of treatment 2—3 weeks.

Contraindicated in hypertensive disease, atherosclerosis, stenocardia, organic diseases of the heart, diarrhea, heightened coagulability of the blood and severe forms of nephritis.

Available in bottles containing 30—50 ml for oral administration and in ampoules containing 1 ml for injections.

To be stored in a cool place protected from light.

Rp Pantocrini 300

DS 30 drops 2—3 times a day (before meals)

Rp Pantocrini 10

D t d N 10 in amp

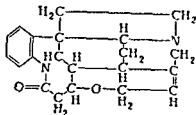
S 1 ml subcutaneously once a day

h) Drugs of the strychnine group

STRYCHNINE (Strychninum)

The principal alkaloid in the seeds of *Nux vomica* (*Strychnos nux vomica*), a tree of the family Loganiaceae found growing in tropical regions of Asia and Africa. *Nux vomica* seeds (semina *Strychni*, semina *Nucis vomicae*) contain other alkaloids besides strychnine (among them brucine). The amount of strychnine and brucine totals at least 2.5%.

Strychnine is a derivative of indole, its structure has not been definitely established but at present the following formula has been accepted



In medical practice strychnine nitrate is used (*Strychninum nitricum*, *Strychnini nitras*).

Strychnine nitrate colourless, lustrous needles unchanged in the air, extremely bitter, sparingly soluble in cold water (1:90) and alcohol, freely soluble in boiling water (1:5), insoluble in ether. Aqueous solutions have a neutral or weak acid reaction. Solutions are sterilized by holding at 100° for 30 min. The 0.1% solution in ampoules is acidified with 0.1 N hydrochloric acid and has a pH of 3.0–3.7.

Strychnine and *nux vomica* preparations stimulate the central nervous system, heightening, first and foremost, the reflex excitability of the spinal cord, in large doses they cause characteristic tetanic convulsions.

In therapeutic doses strychnine has a stimulating effect on the sense organs sharpening vision, taste, hearing and the sense of touch, it stimulates the vaso-motor and respiratory centres, tonicizes the skeletal muscles, as well as the myocardium, and stimulates the metabolic functions. It also heightens the sensitivity of the retina.

The action of strychnine is associated with its facilitation of the transmission of impulses in the intraneuronic synapses. Recent experimental findings show that the action of strychnine is effected predominantly in the region of the so-called intercalated neurons, which play the role of inhibitory cells. The chemical substances formed in these cells have an inhibitory influence on the transmission of impulses in the synapses of the central nervous system. Like curare which hinders the action of the chemical mediator in the region of the neuromuscular synapses, strychnine may possibly hinder the action of the inhibitory factor in the region of the central synapses and in this way have a «stimulating» effect.

Strychnine is used as a tonic in cases of a lowering of metabolic processes, abnormal fatigability, hypotensive disease, weakened cardiac activity as a consequence of intoxication and infection, in some functional ailments of the visual apparatus (amblyopia, amaurosis, etc.), in paresis and paralysis (specifically, that arising from diphtheria in children), in gastric atony, etc.

Prescribed orally (usually in pills) and subcutaneously (in the form of 0.1% solution).

Usual dose for adults 0.0005–0.001 g 2–3 times a day.

Maximal doses for adults (orally and subcutaneously) single — 0.002 g, daily — 0.005 g.

Maximal doses for children 2 years old, single — 0.00025 g, daily — 0.0005 g, 3–4 years, single — 0.0003 g, daily — 0.0006 g, 5–6 years, single —

0.0003 g daily—0.001 g 7—9 years single—0.0006—0.00075 g daily—0.0012—0.0015 g 10—14 years single—0.00075—0.001 g daily—0.0015—0.002 g Children up to 2 years old are not prescribed strychnine

Contraindications hypertensive disease atherosclerosis acute and chronic nephritis hepatitis epilepsy, tetany Basedow's disease

Available in ampoules containing 1 ml 0.1% solution

To be kept locked (List A) in well stoppered bottles or sealed ampoules

The following preparations of nux vomica are also used

Dry extract of nux vomica (*Extractum Strychni siccum* *Extractum nucis vomicae siccum*) Dry light brown powder odourless The aqueous solution (1:10) is turbid and extremely bitter Contains about 16% alkaloids (strychnine and brucine)

Prescribed orally in pills in doses of 0.005—0.01 g

Maximal doses for adults single—0.01 daily—0.03 g

Maximal doses for children 2 years old single—0.0015 g daily—0.005 g 3—4 years single—0.002 g daily—0.006 g 5—6 years single—0.003 g daily—0.009 g 7—9 years single—0.001 g daily—0.012 g 10—14 years single—0.006 g daily—0.018 g Children up to 2 years old are not prescribed nux vomica extract

To be kept locked (List A)

Nux vomica tincture (*Tinctura Strychni* *Tinctura Nucis vomicae*) Transparent brown liquid of extremely bitter taste Prepared from dry extract of nux vomica and 70% alcohol at a rate of 16 g extract per liter of alcohol Contains 0.2% alkaloids (strychnine and brucine)

Used as a general tonic and as bitters to arouse an appetite

Prescribed orally (alone or mixed with other tinctures) in doses of 3—10 drops

Maximal doses for adults single—0.3 ml (15 drops) daily—0.6 ml (30 drops)

Maximal doses for children 2 years old single—1 drop daily—2 drops 3—4 years single—2 drops daily—4 drops 5—6 years single—3 drops daily—6 drops 7—9 years single—4 drops daily—8 drops 10—14 years single—5—6 drops daily—10—12 drops The preparation is not prescribed for children up to 2 years old

Safety precautions must be observed in storage (List B)

SECURININE (*Securininum*)

The alkaloid securinine $C_{13}H_{15}O_2N$ is obtained from the herb *Securinea suffruticosa* Pall of the Spurge family (*Euphorbiaceae*), found growing in the Far East

In medical practice the nitrate of securinine is used (*Securininum natrium*)

White powder with pinkish cream colour tint odourless bitter soluble in water sparingly soluble in alcohol

Stimulates the central nervous system especially heightening the reflex excitability of the spinal cord In the character of its effect securinine is similar to strychnine but is less potent and less toxic (from 8 to 10 times)

Used as a tonic in asthenic conditions neurasthenia accompanied by abnormal fatigability weakness of cardiac activity paresis and flaccid paralysis (including paralysis during the restorative period after poliomyelitis) and sexual impotency arising from functional nervous disorders

Prescribed orally in a dosage of 10—20 drops 0.4% solution 2—3 times a day or subcutaneously in a dosage of 1 ml 0.2% solution once a day (for adults) The course of treatment is for 20—30 days or more

Maximal doses for adults orally single dose—0.005 g daily dose—0.015 g subcutaneously single—0.003 g daily—0.005 g

Contraindications are the same as for strychnine

Available in vials containing 15 ml 0.4% solution (1:250) and in ampoules containing 1 ml 0.2% solution

To be kept locked (List A) in a place protected from light

Rp Sol Securini nitrici 0.4% 150
DS 10—20 drops 2—3 times a day

Rp Sol Securini nitrici 0.2% 10
D t d N 6 in amp
S 1 ml subcutaneously once a day

ECHINOPSINE (Echinopsinum)

Echinopsine is an alkaloid contained in the seeds of the common globe thistle (Echinops Ritro L.)

Echinopsine nitrate (Echinopsinum nitricum), $C_{10}H_9ON \cdot HNO_3$, yellowish amorphous powder, bitter, freely soluble in water and ethanol sparingly soluble in ether Melting point 148—150°

In its pharmacological properties, echinopsine is similar to strychnine it raises the reflex excitability of the spinal cord, tonicizes the skeletal muscles and has a general tonic effect In large doses it causes convulsions

Used in muscular atrophy, peripheral paralysis asthenic conditions with symptoms of hypotonia, etc

Prescribed orally in the form of a 1% aqueous solution, 10—20 drops twice a day, when there is good tolerance the single dose may be increased to 30 drops Subcutaneously, 1 ml 0.25% solution is given once a day The course of treatment lasts 20—30 days When necessary the course is repeated in 1—1½ months

Contraindications stenocardia bronchial asthma, 3rd stage of hypertensive disease

Available in vials containing 30 ml 1% solution and in ampoules containing 1 ml 0.25% solution

To be kept locked (List A) in a cool place, in vials of dark glass or sealed ampoules

Rp Sol Echinopsini nitrici 1% 300
DS 10 drops twice a day

Rp Sol Echinopsini nitrici 0.25% 10
D t d N 10 in amp
S 1 ml subcutaneously once a day

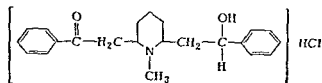
1) Respiratory stimulants

LOBELINE (Lobelinum)

An alkaloid contained in the plant *Lobelia inflata* of the Bellflower family (Campanulaceae) Optically active, the racemate of lobeline is obtained synthetically

In medical practice the hydrochloride of lobeline (Lobelinum hydrochloricum, Lobelini hydrochloridum) is used

Chemically it is 2 (β hydroxyphenetyl)-1 methyl 6 phenacylpiperidine hydrochloride



White or yellowish crystalline powder, odourless, bitter, soluble in 100 parts of water and 15 parts of alcohol Solutions have an acid reaction, they are sterilized by Tyndallization at 60°

Lobeline is a potent respiratory stimulant. Unlike analeptics of the caffeine, pentylenetetrazol and phenamine type the principal manifestation of the central effect of lobeline is the stimulation of respiration, it is not accompanied by pronounced general stimulation or an increase in the capacity for mental and physical work. Lobeline's effect on respiration is transitory, when lobeline is administered intravenously — the usual method — the stimulation of respiration is in the nature of a stiff but short "jolt".

The stimulating effect of lobeline is chiefly of a reflex character and is associated with the excitation of the carotid ganglia. It is partly due to a direct influence on the respiratory centre. The excitation of the carotid ganglia is one of the manifestations of lobeline's ganglionic action. In the proper doses, lobeline stimulates the ganglia of the autonomic nervous system simultaneously. There is an excitation of the carotid ganglia and the chromaffinic tissues of the adrenals, which in the embryological and physiological respect are closely related to the autonomic ganglia.

Under the influence of lobeline, the other centres of the oblongata are stimulated along with the respiratory centre. Stimulation of the centre of the vagus nerve leads to a retarding of the pulse and a lowering of the arterial pressure. Later the arterial pressure may rise somewhat, this depends on the contraction of the vessels, which is a consequence of the stimulating effect of lobeline on the sympathetic ganglia and adrenals. In large doses lobeline excites the vomiting centre, and causes paralysis of the heart, severe depression of respiration and tonic-clonic spasms.

Indications for the use of lobeline: stoppage of breathing, or respiratory weakness in the absence of significant disorders of the cardiovascular system.

Lobeline is particularly indicated in reflex stoppages of respiration (on inhaling irritating substances and in the first stage of anesthesia, etc.)

The drug is also used in asphyxia neonatorum.

When respiration weakens or stops as a consequence of progressive exhaustion of the respiratory centre the administration of lobeline is not indicated.

Lobeline is usually administered in the form of intravenous injections, less frequently it is administered intramuscularly.

Adults are prescribed 0.003—0.005 g (0.3—0.5 ml 1% solution) intravenously or intramuscularly, children are prescribed 0.001—0.003 g (0.1—0.3 ml 1% solution), depending on the age.

When lobeline is administered intravenously, the injection must be slow (1 ml in 1—2 min), when injected rapidly, a temporary cessation of respiration (apnea) sometimes ensues and side effects develop in the cardiovascular system (bradycardia and impairment of conductivity).

Lobeline is likewise used for determining the speed of the blood flow for diagnostic purposes. The method is based on the determination of the time that elapses from the moment the drug is injected into the vein (0.003—0.005 g) till the appearance of the first signs of dyspnea. This method requires the rapid intravenous injection of lobeline, and consequently the possibility of side effects developing in the cardiovascular system must be borne in mind.

More precise results are obtained when cytolon is used for this purpose.

Maximal doses for adults intravenously, single dose — 0.005 g, daily dose — 0.01 g, intramuscularly, single dose — 0.01 g, daily dose — 0.02 g.

Maximal doses for children (intravenously and intramuscularly) up to 6 months old, single — 0.001 g, daily — 0.002 g, from 6 months to 1 year, single — 0.0015 g, daily — 0.003 g, 2 years, single — 0.002 g, daily — 0.004 g, 3—4 years, single — 0.002 g, daily — 0.004 g, 5—6 years, single — 0.0025 g, daily — 0.005 g, 7—9 years, single — 0.003 g, daily — 0.006 g, 10—14 years, single — 0.004 g, daily — 0.008 g.

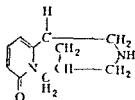
Available in ampoules containing 1 ml 1% solution.

To be stored in a place protected from the light, observing safety precautions (List B).

Rp Sol Lobelini Hydrochlorici 1% 10
 D t d N 6 in amp
 S For intravenous injections (0.3—0.5 ml)

CYTITON (Cytitonum)

0.15% solution of the alkaloid cytisine, which is contained in the seeds of the broom (*Cytisus laburnum* L.) and thermopsis (*Thermopsis lanceolata*, R Br.), both plants belonging to the family Leguminosae



Cytisine

Cytiton is a transparent, colourless liquid pH=8.2—8.8 Sterilized by holding at 100° for 30 min

Cytisine, like lobeline, excites the ganglia of the autonomic nervous system and related tissues the chromaffine tissue of the adrenals, and the carotid ganglia. As the result of the excitation of the carotid ganglia and of cytisine's direct action on the respiratory centre, there is an intense stimulation of respiration. The action is transitory—in the nature of a "jolt"—just as when lobeline is administered.

Cytisine stimulates the respiration to a greater degree than lobeline, as a consequence of the strong excitation of the sympathetic ganglia and adrenals a considerable elevation of the arterial pressure is observed.

For medical purposes cytiton, a 0.15% solution of cytisine, is used its potency (as manifested in its influence on respiration) is approximately that of a 1% solution of lobeline.

Cytiton is used in cases of reflex stoppage of breathing during operations or as a result of trauma, in cases of weakening of respiratory and cardiovascular activity in various intoxications (poisoning with carbon monoxide, hydrocyanic acid, narcotics, etc.) as well as in infectious diseases, in shock and collapsoid conditions, in depressed respiration and circulation in the postoperative period, in asphyxia neonatorum.

Cytiton is likewise used in determining the speed of the blood flow. The method is based on the determination of the time that elapses from the moment cytiton is injected into the cubital vein until the first deep inspiration. The determination is more demonstrative than when lobeline is injected since the stimulation of respiration is manifested more distinctly. The change in respiration is easily recorded on a kymograph.

For this purpose, an injection of 0.7—1 ml of cytiton is usually given (0.015 ml per kg of body weight).

For therapeutic purposes cytiton is administered intravenously or intramuscularly. Doses for adults 0.5—1 ml. Doses for children up till 12 months old, 0.1—0.15 ml, from 2 to 5 years, 0.2—0.3 ml, from 6 to 12 years, 0.3—0.5 ml.

When indicated the injection of cytiton may be repeated in 15—30 min.

Maximal doses for adults (intravenously and intramuscularly) single—1 ml daily—2 ml.

Maximal doses for children (intravenously and intramuscularly) Up to 6 months old, single—0.15 ml, daily—0.3 ml, from 6 months to 1 year, single—0.15 ml, daily—0.3 ml, 2 years, single—0.2 ml, daily—0.4 ml, 3—4 years single—0.25 ml, daily—0.5 ml, 5—6 years single—0.3 ml.

daily — 0.6 ml, 7—9 years, single — 0.4 ml, daily — 0.8 ml, 10—14 years,
single — 0.6 ml daily — 1.2 ml

Because of cytilon's ability to raise the arterial pressure, it should not be used in cases of pronounced atherosclerosis and hypertension, hemorrhage from the great vessels or pulmonary edema

Available in ampoules of 1 ml.

To be stored in sealed ampoules, observing safety precautions (List B)
Cytisine powder is to be kept locked (List A).

Rp Cytilon 10

D t d N 6 in amp

S 1 ml intravenously (for an adult)

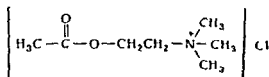
Chapter II

MEDICINAL AGENTS ACTING PREEMINENTLY IN THE REGION OF THE ENDINGS OF THE EFFERENT (CENTRIFUGAL) NERVES

I. SUBSTANCES ACTING PREEMINENTLY ON ORGANS INNERVATED WITH AUTONOMIC NERVES

A. Acetylcholine and cholinomimetic substances

ACETYLCHOLINE CHLORIDE (*Acetylcholinum chloratum*)



Synonyms *Acecoline*, *Acetylcholini chloridum*

Colourless crystals which deliquesce in the air, freely soluble in water and alcohol

Acetylcholine is formed in the bodies of man and animals during the process of neural activity. As a medicinal agent the chloride¹ is used, it is prepared synthetically.

Acetylcholine is a quaternary monoammonium compound. It is a chemically unstable substance which is easily hydrolyzed in the body by the special tissue enzyme, cholinesterase, into choline and acetic acid.

Acetylcholine plays an important role in the body's vital activities. It promotes the transmission of neural impulses in the central nervous system, the autonomic ganglia, and the endings of the parasympathetic division of the nervous system and the motor nerves. Acetylcholine is the chemical transmitter (mediator) of the neural impulse, the nerve fibres for which it is the mediator are termed cholinergic, while the biochemical systems of the body tissues interacting with it are called cholinoreactive systems (or cholinorecep

¹ The iodide can be used on a par with the chloride but one must take into account the fact that the molecular weight of acetylcholine chloride is 181.66 while the molecular weight of the iodide is 273.12

tors) The cholinoreactive tissue systems innervated with endings of the postganglionic cholinergic nerves (the heart smooth muscles and glands) are termed m cholinoreactive ("muscarine sensitive"), those situated in the region of the ganglionic synapses and in the somatic neuromuscular synapses are termed n cholinoreactive ("nicotine sensitive") (S V Anichkov's system). This division is based on the peculiarities of the action of acetylcholine on these biochemical systems: in the first case it resembles muscarine, in the second case nicotine. The effect of acetylcholine on the m cholinoreactive systems like the effect of muscarine is abolished by atropine; its effect on the n cholinoreactive systems of the ganglionic synapses is abolished by the so-called "ganglion blocking substances" (see p 107) and that on the n cholinoreactive systems of the striate muscles by curare drugs (see p 123).

The question of the character of the reaction between the synaptic apparatus of the central nervous system and acetylcholine is as yet insufficiently clear. Experimental findings indicate that the biochemical systems of the interneuronic connections of the brain, especially the subcortical elements and the posterior lobe of the hypophysis, react for the most part like n cholinoreactive systems. At the same time there are facts indicating the possibility of their reacting like muscarine-sensitive systems.

The peripheral muscarine-like action of acetylcholine is manifested in a retarding of heart contractions, dilation of the peripheral blood vessels and lowering of arterial pressure, intensification of the peristalsis of the stomach and intestine, contraction of the bronchi, uterus, gall bladder and bladder muscles, intensification of secretion by the digestive, bronchial, sweat and lacrimal glands, and contraction of the pupil (miosis). The miotic effect is due to the increased contraction of the sphincter pupillae, which is innervated with postganglionic cholinergic fibres of the oculomotor nerve. Simultaneously there is a spasm of accommodation as a result of the contraction of the ciliaris muscle and the relaxation of Zinn's ligament.

The contraction of the pupil caused by acetylcholine and cholinomimetic substances is usually accompanied by a lowering of intraocular pressure. This effect is partly explained by the fact that when the pupil contracts and the iris is flattened, the canal of Schlemm and the canals of Fontana dilate, thus making for a better outflow of liquid from the interior of the eye. There are however grounds for believing that other mechanisms which have not been sufficiently studied as yet also play a part in lowering intraocular pressure.

The peripheral nicotine-like action of acetylcholine is accompanied in small doses by a facilitation of the transmission of neural impulses from the preganglionic fibres to the postganglionic ones in the autonomic ganglia, as well as from the motor nerves to the striated muscles. In large doses acetylcholine blocks the transmission of neural impulses.

In small doses acetylcholine also facilitates the transmission of impulses in the central nervous system, while in large doses it inhibits this transmission.

As a medicinal agent acetylcholine is used in spasms of the peripheral vessels (endarteritis, intermittent lameness, trophic disorders in stumps, etc.) in spasms of the retina, arteries and sometimes in glaucoma, in atony of the intestine and bladder. It is likewise used in the auricular form of paroxysmal tachycardia.

Acetylcholine has a transitory effect since it is quickly destroyed in the body; it is ineffective when administered by mouth.

Intravenous administration is impermissible because of the possibility of a sharp fall in the arterial pressure and stoppage of the heart.

Acetylcholine is widely used in the laboratory in carrying out pharmacological and physiological investigations.

For therapeutic purposes the drug is prescribed subcutaneously or intramuscularly in a dosage of 0.05 or 0.1 g (for adults). If necessary, injections can be given 2-3 times a day. When giving injections care must be taken that the needle does not enter a vein.

Maximal doses subcutaneously and intramuscularly for adults single — 0.1 g, daily — 0.3 g

Acetylcholine is contraindicated in bronchial asthma, stenocardia, atherosclerosis, organic heart disease and epilepsy

When using acetylcholine for therapeutic purposes, it must be borne in mind that the drug causes a contraction of the coronary vessels of the heart

If there should be an overdosage of acetylcholine, 1 ml of 0.1% atropine solution should immediately be given intravenously or subcutaneously (the injection should be repeated if necessary)

Available in 5 ml ampoules containing 0.1 or 0.2 g of dry acetylcholine, and in vials containing 1 g The drug is dissolved immediately before use the ampoule is opened and the necessary amount of sterile distilled water (2–5 ml) is added with a syringe

Solutions cannot be sterilized On standing, solutions decompose

To be stored in sealed ampoules, observing safety precautions (List B)

Rp Acetylcholini chlorati 0.1

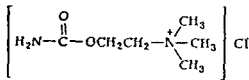
D t d N 3 in amp

S Dissolve in 1–2 ml sterile distilled

water, administer 0.5–1 ml subcutaneously

CARBOCHOLINE CARBACHOLINE (Carbocholinum Carbacholinum)

Carbamylcholine chloride



Synonyms Carbacholum Carbamylcholine Carcholin Choryl Doryl, Dura choline, Enterotonin, Iestryl, Lentin, Moryl, Tonocholin

White crystalline powder with faint odour resembling that of aliphatic amines, hygroscopic, very freely soluble in water, sparingly soluble in alcohol practically insoluble in ether and chloroform Melting point 203–205° (decomp) Solutions are sterilized by holding at a temperature of 100° for 30 min

In chemical structure and pharmacological properties carbocholine is similar to acetylcholine, but it is more potent and its effect is of greater duration since it is not hydrolyzed by cholinesterase Thanks to the drug's stability, it can be administered not only parenterally but orally as well

Carbocholine is used in atony of the intestine and bladder particularly in the postoperative period, in early forms of hypertensive disease, in paroxysmal tachycardia, endarteritis obliterans and glaucoma It is likewise used to stimulate labour

Carbocholine is prescribed in the following doses for adults orally from 0.0005 to 0.001 g (0.5–1 mg), subcutaneously and intramuscularly, from 0.0001 to 0.00025 g (0.1–0.25 mg)

Carbocholine can be administered 2–3 times daily for a lengthy period (2–3 weeks) Care must be taken, however, in respect to the dosage Great caution must be observed in the case of intravenous administration (0.00005 g = 0.05 mg), the injection must be given very slowly When employing carbocholine it should be borne in mind that like acetylcholine it can cause the coronary vessels of the heart to contract

In glaucoma 0.5–0.75% solutions of carbocholine are instilled into the conjunctival sac 2–6 times a day

Maximal doses for adults single, orally — 0.001 g, single subcutaneously — 0.0005 g daily, orally — 0.003 g daily, subcutaneously — 0.001 g

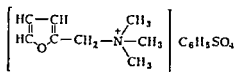
Contraindications stenocardia pronounced atherosclerosis bronchial asthma epilepsy Carbocholine is also contraindicated if there should be pylorism diarrhea or marked bradycardia when the drug is given in the usual doses. When carbocholine is taken a feeling of fever is sometimes observed, along with salivation and nausea. If the dosage is correct these symptoms pass away of themselves. In case of pronounced side effects atropine should be given intravenously or subcutaneously (1 ml of 0.1% solution), if necessary the injection is repeated.

Available in powder form, in tablets of 0.001 g and in ampoules containing 1 ml 0.01 or 0.025% solution.

To be kept locked (List A) in well stoppered glass bottles in a cool place protected from light.

BENZAMON (Benzamonum)

Furfuryltrimethylammonium benzenesulfonate



White crystalline substance, freely soluble in water and alcohol, insoluble in ether. Melting point 133—134°. Solutions are sterilized by holding at 100° for 30 min.

Similar in effect to acetylcholine and carbocholine, potent miotic, lowers the intraocular pressure.

Employed in the form of aqueous solutions and ointments in the treatment of glaucoma. In the subcompensated form a 3% solution is used, and in the decompensated form a 10% solution.

Drops are instilled into the conjunctival sac 2 to 6 times a day, depending on the peculiarities of the case.

When using benzamon as when using other miotics, there may be pain in the eyes and the superciliary region in individual cases, along with a deterioration of vision as a consequence of a spasm of accommodation. In persons with a heightened sensitivity to benzamon follicular catarrh of the conjunctiva may develop.

To be kept locked (List A)

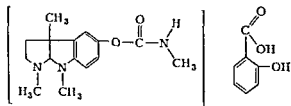
B Anticholinesterase agents

PHYSOSTIGMINE, ESERINE (Physostigminum Eserinum)

Physostigmine or eserine, is the principal alkaloid contained in Calabar Beans — the seeds of *Physostigma venenosum*, a West African plant of the family Leguminosae.

Chemically, physostigmine is a derivative of indole, and it also contains a urethan group.

In medicine the salicylate of physostigmine (eserine) (*Physostigminum s Eserinum salicylicum*, *Physostigmini s Eserini salicylas*) is used.



Colourless crystals sparingly soluble in water (1 : 100) soluble in alcohol (1 : 12) Powder and solutions turn red and become inactive on exposure to light and air Solutions are prepared aseptically or are Tyndallized

Physostigmine is a representative of the so called "anticholinesterase substances" One of the principal properties of these substances is their ability to depress the activity of cholinesterase in this way protecting acetylcholine from rapid hydrolysis

As a result of this property anticholinesterase substances bring about effects outwardly similar to those produced by acetylcholine and cholinomimetic substances Along with their influence on cholinesterase these substances also act directly on the tissues

The pharmacological antagonist of physostigmine is atropine

Physostigmine salicylate is mainly used in ocular practice for contracting the pupil and lowering the intraocular pressure in glaucoma 1—2 drops of 0.2%—1% solution are instilled into the conjunctival sac 1—6 times a day Contraction of the pupil usually sets in within 5—15 min and persists 2—3 hours or more In keratitis ointments containing 0.2—0.25% physostigmine are used Eye-drops are better prepared with a 2% solution of boric acid Physostigmine has a stronger effect in glaucoma than pilocarpine but it sometimes causes pain in the eye and superciliary region due to the sharp contraction of the iris for that reason physostigmine is used for the most part in acute glaucoma and in cases in which pilocarpine is not sufficiently effective A combination of 0.25% physostigmine and 1% pilocarpine gives a good effect

Physostigmine is likewise occasionally employed in the nervous diseases clinic in neuromuscular disorders as well as in intestinal paresis (0.5—1 ml of 0.1% solution subcutaneously) Its synthetic substitute proserine is more widely used for these purposes

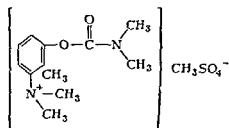
Maximal doses for adults (subcutaneously) single — 0.0005 g daily — 0.001 g

To be kept locked (List A), in well stoppered bottles of amber glass in a place protected from light

Solutions are dispensed in bottles of amber glass

PROSERINE (Proserinum)

(m Hydroxyphenyl) trimethylammonium methylsulfate dimethylcarbamate (or dimethyluretan)



Synonyms Eustigmin Myostigmine Neoeserin Neostigmini methylsulfas Neostigmine methylsulfate Prostigmin methylsulfate Stigmosan Syntostigmin Vasostigmin

White crystalline powder odourless bitter taste hygroscopic freely soluble in water (1 : 10) and in alcohol (1 : 5) almost insoluble in ether Acquires a pink tint under the influence of light Melting point 142—146° pH of 0.05% aqueous solution 6.5—7.5 Solutions are sterilized by holding at 100° for 30 min

Proserine is a synthetic substance It differs from physostigmine in chemical structure in the first place it is a quaternary ammonium compound and besides that it does not contain the indole nucleus characteristic of physostigmine

In its pharmacological properties, especially its peripheral effects, proserine is nevertheless similar to physostigmine it also reduces the activity of cholinesterase and hinders the hydrolysis of acetylcholine. Proserine is more stable than physostigmine.

Proserine is used in myasthenia motor disorders after cerebral trauma, and paralysis in the restorative period after tuberculous meningitis, poliomyelitis, encephalitis, etc., in atrophy of the ocular nerve and neuritis, for the prevention and treatment of atony of the intestine and bladder. The drug is also employed to stimulate labour. In ocular practice proserine is prescribed in order to contract the pupil and lower intraocular pressure in patients with glaucoma.

Proserine is an antagonist of curarelike drugs whose action is associated with their concurrent relations with acetylcholine in the region of the neuromuscular synapses (tubocurarine, diptacine, paramylon, etc.). In large doses proserine itself may cause an impairment of neuromuscular conductivity due to the accumulation of acetylcholine and persistent depolarization in the region of the synapses (see p. 124).

Proserine is usually administered orally or subcutaneously.

Prescribed in powders or tablets in a dosage of 0.01–0.015 g 2–3 times a day for adults, children up to 10 years old are given a daily dose of 0.001 g for each year of their age, children more than 10 years old are given a maximal daily dose of 0.01 g (10 mg).

Subcutaneously, adults are given injections of 0.0005 g (0.5 mg = 1 ml 0.05% solution) once or twice daily, children are prescribed 0.1 ml 0.05% solution for each year of their age but not more than 0.75 ml for one injection.

Treatment of myasthenia with proserine is lengthy, in other diseases the course of treatment is for 25–30 days. If necessary the course of treatment is repeated after a break of 3–4 weeks.

In uterine inertia proserine is administered orally in doses of 0.003 g (3 mg) 4–6 times at intervals of 40 min. During the interval between the second and third powder 0.01–0.02 g phenamine can be given orally. Proserine is also given subcutaneously to stimulate labour, 1 or 2 injections of 1 ml 0.05% solution (the second injection 1 hr after the first), simultaneously with the first injection a single injection of 1 ml 0.1% atropine solution is given subcutaneously.

In ocular practice a 0.5% solution is used, 1–2 drops being instilled into the conjunctival sac 1–4 times a day.

When neostigmine is employed to abolish the effect of curarelike drugs it is administered intravenously in relatively large doses 0.001 g (1 mg) every 10 min until the desired effect is obtained (Y. N. Meshalkin and V. P. Smolnikov). The total dose usually comes to 2.5–5 mg. Preliminarily (5 min before hand) atropine is given intravenously (0.6–1.2 mg in 20 ml distilled water).

Maximal doses for adults: single dose, subcutaneously — 0.0005 g (0.5 mg), orally — 0.015 g (15 mg), daily dose, subcutaneously — 0.001 g, orally — 0.05 g.

Maximal daily doses for children: from 6 months to 1 year old orally — 0.001 g, subcutaneously (0.05% solution) — 0.1 ml (0.05 mg), 2 years orally — 0.002 g, subcutaneously — 0.2 ml (0.1 mg), 3–4 years, orally — 0.003 g, subcutaneously — 0.3 ml (0.15 mg), 5–6 years orally — 0.005 g, subcutaneously — 0.5 ml (0.25 mg), 7–9 years orally — 0.007 g, subcutaneously — 0.6 ml (0.3 mg), 10–14 years orally — 0.01 g, subcutaneously — 0.75 ml (0.375 mg). Infants up to 6 months old are not prescribed proserine.

Proserine is contraindicated in epilepsy, bronchial asthma, stenocardia and pronounced atherosclerosis. In cases of overdosage or poor tolerance atropine is employed as a pharmacological antagonist.

Available in powder form in tablets of 0.015 g and in ampoules containing 1 ml 0.4% solution.

To be kept locked (List A) in well stoppered bottles of amber glass or in sealed ampoules in a place protected from light

Rp Proserini 0015
D t d N 20 in tabul
S 1 tablet twice a day

Rp Sol Proserini 005% 10
D t d N 6 in amp
S 1 ml subcutaneously once or twice daily (for adult), 0.4 ml subcutaneously for 5 year old child

GALANTHAMINE (Galanthaminum)

An alkaloid isolated from the bulbs of Voronov's Snowdrop (*Galanthus Woronowi* A. Los), a plant of the Amaryllis family (Amaryllidaceae), it is also contained in other species of snowdrops and closely related plants. In the Bulgarian People's Republic the same alkaloid has been isolated from *Galanthus nivalis* var. *gracilis* and named Nivaline.

In medical practice the hydrobromide of galanthamine is used white fine crystalline powder of bitter taste, sparingly soluble in water. Melting point 246—247° (decomp).

Aqueous solutions are stable on standing they are sterilized by holding at 100° for 30 min.

The chemical structure of galanthamine has not been definitely established. In its pharmacological properties, galanthamine is similar to physostigmine. It is a potent inhibitor of cholinesterase and heightens the body's sensitivity to acetylcholine. It facilitates the transmission of impulses in the neuromuscular synapses and restores neuromuscular conductivity blocked by curarelike drugs having a concurrent type of action (tubocurarine, dypalazine, etc.), the action of depolarizing substances (ditilin) is intensified by galanthamine. Galanthamine facilitates the transmission of impulses in the synapses of the central nervous system and intensifies excitatory processes. The administration of galanthamine raises the tone of the smooth muscles and intensifies secretion by the glands. Like physostigmine, it causes a contraction of the pupil; it should, however, be noted that when galanthamine solutions are instilled into the conjunctival sac a transitory edema of the conjunctiva develops.

The peripheral muscarine-like effects of galanthamine are abolished by atropine while the nicotine-like effects are abolished by curarelike and ganglion blocking substances. Galanthamine is less toxic than physostigmine.

The use of galanthamine in medicine is mainly associated with its ability to improve the transmission of impulses in the synapses of the central and peripheral nervous systems and heighten the activity of the voluntary muscles. It is prescribed in myasthenia, myopathy and motor and sensory impairment arising from diseases and traumatic injuries of the nervous system, etc. Galanthamine is very effective in the restorative residual period of acute anterior poliomyelitis and in children's cerebral palsies (M. B. Eridimova, Y. N. Pravdina, Vinarskaya, N. A. Shenk et al.). The use of galanthamine particularly in combination with other measures (therapeutic physical culture, etc.), often leads to the improvement or restoration of motor processes and a general improvement in patient's condition.

Galanthamine is administered subcutaneously in the form of an aqueous solution. The dosage must be individualized, depending on the patient's age, the character of the disease, the effectiveness of the drug and the extent to which it is tolerated. The single dose for adults is usually from 0.0025 g (2.5 mg) to 0.01 g (10 mg), i. e., 0.25—1 ml of 1% solution. Administered once or when necessary, twice a day.

Maximal doses for adults single—0.01 g (10 mg), daily—0.02 g (20 mg).

Children are usually prescribed galanthamine in the following doses

Age	Dose
1-2 years	0.00025-0.0005 g (0.1-0.2 ml 0.25% solution)
3-5 "	0.0005 -0.001 " (0.2-0.4 " " " ")
7-8 "	0.00075-0.002 " (0.3-0.8 " " " ")
11 "	0.00125-0.003 " (0.5 ml 0.25%-0.6 ml 0.5% solution)
14 "	0.00175-0.005 " (0.7 " " -1 " " ")
16 "	0.002 -0.007 " (0.2-0.7 ml 1% solution)

Administration of the drug is commenced with the smaller dose gradually increasing it. The length of treatment is individualized depending on the peculiarities of the case and the efficacy of treatment. In mild cases a single course of 3-10 injections is often sufficient. In other cases more lengthy treatment is necessary - up to 25 injections and with a repetition of the course. In mild cases injections can be given 2-3 times a week.

When the dosage is correct galanthamine is tolerated well. In cases of overdosage and of heightened individual sensitivity side effects such as salivation, bradycardia, vertigo etc., are possible. When side effects are pronounced atropine is given subcutaneously or intravenously (1 ml 0.1% solution for adults). If there is heightened sensitivity the dose of galanthamine for subsequent injections is reduced.

Galanthamine like other anticholinesterase drugs is contraindicated in epilepsy, hyperkinesia, bronchial asthma, stenocardia and bradycardia.

Available in ampoules containing 1 ml 0.25, 0.5 or 1% solution.

To be kept locked (List A) in sealed ampoules.

Rp Sol Galanthamini 1% 10

D t d N 6 in amp

S 0.5 ml intravenously once or twice a day (for adult)

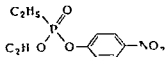
Rp Sol Galanthamini 0.25% 10

D t d N 6 in amp

S 0.5 ml intravenously once or twice a day (for 8 year old child)

PHOSPHACOL (Phosphacolum)

Diethyl p nitrophenyl phosphate



Synonyms: Mintacol, Miotisal, Paraaxon, Soluglaucit

Transparent yellowish oily liquid, sparingly soluble in water (1:1000), freely soluble in alcohol, ether and benzene. Aqueous solutions are prepared aseptically.

Phosphacol is a representative of a group of organic esters of phosphoric acid having anticholinesterase activity. The drugs armine and pyrophos also belong to this group.

The anticholinesterase action of these compounds is manifested very strongly; they are considerably more potent than physostigmine and proserpine and firmly bind cholinesterase. In spite of the fact that they themselves are quite

rapidly excreted from the body the effects they bring about persist for many hours and even days, since a long time is required for the restoration of the cholinesterase activity of the tissues

Changes in the body's activities caused by these compounds coincide to a considerable degree with the changes caused by physostigmine and other anticholinesterase substances. Because of their intense and lasting miotic effect they have found application as miotics and antiglaucoma agents

Phosphacol is administered in the form of aqueous solutions of different strength 0.02% (1:5,000), 0.0133% (1:7,500) and 0.01% (1:10,000)

In chronic glaucoma, phosphacol is prescribed in solutions of 1:7,500—1:10,000 beginning with 2 drops twice a day. Can be used in combination with pilocarpine or other miotics. Subsequently, depending on the effect, the frequency of instillation is reduced, or if a solution of this strength should not be sufficiently active, a shift is made to a 1:5,000 solution, 2 drops being instilled twice a day. In acute attacks of glaucoma a 1:5,000 solution is used

As a miotic phosphacol is employed in perforation of the cornea, prolapse of the lens and other cases when it is necessary to achieve intense and lengthy contraction of the pupil, as well as for diminishing the effect of atropine on the eye (phosphacol reduces the dilation of the pupil and the paralysis of accommodation caused by atropine). For these purposes 1—2 drops of a 1:7,500 solution is instilled into the conjunctival sac. In pediatric practice a 1:10,000 solution is used

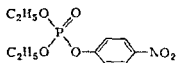
Side effects from phosphacol may be observed in individual cases, just as when physostigmine is used: twitching of the lids, headache, pain in the eye and at times transitory hyperemia of the mucous membrane of the eye. Side effects pass away of themselves. In order to avoid such symptoms more than 2 drops should not be instilled at a time. After each instillation it is recommended that the region of the lacrimal sac should be pressed with the finger for 2—3 min to prevent the solution from entering the nasolacrimal duct and being absorbed

Available in vials containing 10 ml of 1:5,000, 1:7,500 or 1:10,000 solution. To be kept locked (List A) in a cool place

Rp Sol Phosphacoli 0.01% (1:10,000) 10.0
DS Eye drops 2 drops twice a day (in glaucoma)

ARMINE (*Arminum*)

Ethyl para nitrophenyl ester of ethylphosphinic acid



Transparent yellowish liquid sparingly soluble in water. Potent anticholinesterase agent. Closely related to phosphacol and pyrophos in its effect and mode of action

Like phosphacol armine is used as a miotic and antiglaucomatous agent. Prescribed in the form of eye drops in a concentration of 0.005% (1:20,000), 1—2 drops 2—3 times a day. In some cases the effect is more pronounced than that from phosphacol. Can be used in combination with other miotics

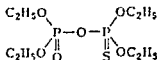
After each instillation of armine the region of the lacrimal sac must be pressed with the finger for 2—3 min to prevent the solution from entering the nasolacrimal duct

Available in vials containing 10 ml of 0.005% solution
To be kept locked (List A) in a place protected from light

Rp Sol Armini 0.005% 10.0
DS Eye drops 1—2 drops 2—3 times a day (in glaucoma)

PYROPHOS Phosarbin

Tetraethyl ester of monothiopyrophosphoric acid



Colourless liquid specific odour resembling that of hydrogen sulphide freely soluble in fats and oils (liquid petrolatum persic oil), sparingly soluble in water (1:1000). Aqueous solutions are unstable the drug being rapidly hydrolyzed.

Pyrophos is a potent anticholinesterase agent closely related to phosphacol and armine in its effect and mode of action. Like those drugs it is also employed as a miotic and antiglaucomatous agent.

Used in the form of oil solutions (in liquid petrolatum or persic oil) in a concentration of 0.01% (1:10000) 2 drops are instilled into the affected eye 2-3 times a day.

Headache and pain in the eye may be observed when pyrophos is used. Prolonged use may give rise to an eczematous irritation and slight edema of the lids.

Available in vials containing 10 ml of 0.01% solution. To be locked (List A) in a place protected from light.

C Cholinolytic agents acting preeminently in the region of the peripheral m-cholinoreactive systems

The term cholinolytic agents¹ is applied to substances that weaken or prevent the reaction between acetylcholine and the cholinoreactive systems of the body. By blocking the cholinoreactive systems they have an effect which is the opposite of that caused by acetylcholine.

In accordance with the division of the cholinoreactive systems into m and n cholinoreactive (see p. 88) cholinolytic substances are also divided into those with a predominant m or n cholinolytic effect. Such a division accords with the fairly high selectivity of the substances in each of these groups. In their action it must however be borne in mind that to a certain degree m cholinolytic substances lower the reactivity of the nicotine sensitive systems of the body while n cholinolytic substances lower the reactivity of the muscarine sensitive systems. Among substances having high selective m cholinolytic activity are atropine and a number of related alkaloids and synthetic compounds.

In accordance with the peculiarities of the peripheral n cholinoreactive systems n cholinolytic substances are divided into two groups. Substances acting chiefly in the region of the ganglionic synapses are put in a special group termed "ganglion blocking substances" because of the peculiarities of their effect and of their therapeutic use (see p. 107). Substances acting chiefly in the region of the somatic neuromuscular synapses are put in a group termed curare like substances (see p. 123).

Cholinolytic substances also have an influence on the central cholinoreactive systems. Substances which have a central cholinolytic action and which are used in the treatment of parkinsonism and other diseases of the extrapyramidal system have been put in a special group and are classed as anticonvulsants.

¹ The term cholinolytic agents is used in the literature. It should be noted however that these substances do not cause a change (lysis) of acetylcholine. It would therefore be more correct to speak of them as choline blocking or antiacetylcholine agents.

(see "Substances Used for the Treatment of Parkinsonism," p 64) Lately "central cholinolytics" have also found application as neuroplegic substances (see Amizyl, p 36)

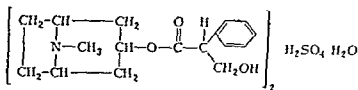
It must be borne in mind that it is not only the substances included in the groups enumerated that possess cholinolytic properties, to a certain degree these properties are possessed by some antihistamines (dimedrol, promethazine, fenethazine), local anesthetics and other substances

a) Substances of natural origin (alkaloids of the atropine and platyphylline group and plants containing them)

ATROPINE (Atropinum)

An alkaloid contained in various plants of the Nightshade family (Solanaceae). Belladonna (*Atropa belladonna* L.) Henbane (*Hyoscyamus niger* L.) and various species of Thorn apple (*Datura stramonium* L.) and others

In medical practice the sulphate of atropine is used (Atropinum sulfuricum, *Atropini sulfas*) Chemically this is the sulphate of the ester of the amino alcohol, tropine, and tropic acid



White, crystalline or granular powder; odourless, freely soluble in water and alcohol Melting point 191—195° Solutions have a neutral reaction, they are sterilized by holding at 100° for 30 min.

Atropine is optically inactive, it is a racemic substance consisting of the extremely potent levorotatory and the slightly active dextrorotatory isomers The levorotatory isomer is called hyoscyamine, it is approximately twice as potent as atropine The natural alkaloid contained in plants is hyoscyamine; during the chemical processing of the plants in order to isolate the alkaloid it is largely converted into the racemic form — atropine

The principal pharmacological property of atropine is its ability to block the m cholinoreactive systems of the body By blocking these systems, atropine renders them insensitive to acetylcholine, which is formed in the region of the endings of the postganglionic parasympathetic (cholinergic) nerves The effects of atropine are therefore the opposite of those observed when the parasympathetic nerves are stimulated

The administration of atropine causes a reduction of secretion by the salivary, gastric and sweat glands (the latter have a sympathetic cholinergic innervation) and by the pancreas, there is likewise an acceleration of cardiac contractions (as a consequence of the diminution of the inhibitory action of the vagus on the heart), and a lowering of the tone of the smooth muscle organs (the bronchi, the organs of the abdominal cavity, etc)

The effect of atropine is particularly pronounced if the smooth musculature is in a state of spasm

Under the influence of atropine there is a marked dilation of the pupils The mydriatic effect results from the relaxation of the sphincter pupillae Simultaneously with the dilation of the pupil there may be an elevation of the intraocular pressure Relaxation of the ciliary muscle of the ciliary body leads to paralysis of accommodation

Atropine has a weak effect on the n cholinoreactive systems of the autonomic ganglia

Atropine's effect on the central nervous system is complicated. It stimulates the cerebral cortex and causes motor and psychic excitement in large doses. It may cause marked unrest and convulsions. In therapeutic doses atropine stimulates respiration but large doses may give rise to respiratory paralysis.

Atropine also has a central cholinolytic effect. In patients with parkinsonism it causes an abatement of tremor and muscular tension. It is however not sufficiently active. At the same time its strong influence on the peripheral cholinolytic systems leads to a number of complications (dryness in the mouth, palpitation etc.) making it difficult to use atropine for these purposes over a lengthy period of time (see "Substances used for the treatment of parkinsonism" p. 64).

Atropine is used in ulcer of the stomach and duodenum, pylorospasm, cholecystitis, cholelithiasis, spasms of the intestine and urinary tract and bronchial asthma. It is likewise used to limit the secretion of the salivary, gastric and bronchial glands. It is given in bradycardia resulting from heightened excitability of the vagus nerve and in atrioventricular heart block (in cases with a very slow rhythm of the ventricles). Atropine is used quite frequently in stenocardia and myocardial infarction.¹

Atropine is often employed in combination with analgetics (promedol etc.) in cases of pain associated with spasms of the smooth muscles.

Due to its ability to reduce secretion by the sweat glands, atropine is sometimes used in cases of sudoresis. In ocular practice it is employed to dilate the pupils for diagnostic purposes (for determining true refraction, examining the eyeground etc.) and also in the therapy of inflammatory diseases (iritis, iridocyclitis, keratitis etc.). The relaxation of the eye muscles induced by atropine ensures functional rest and helps overcome the pathological process.

As an antidote, atropine is prescribed in cases of poisoning with acetylcholine, carbacholine and various cholinomimetic and anticholinesterase substances as well as poisoning with morphine and other analgetics. Atropine is often used along with morphine (or omnopon) in order to diminish the side effects caused by the latter associated with stimulation of the vagus.

Atropine is usually prescribed orally, subcutaneously or locally (in the form of eye drops). Orally, adults are given doses of 0.0002 g (0.25 mg), 0.0005 g (0.5 mg) or 0.001 g (1 mg) in powders or 0.1% solution once or twice daily. Subcutaneously 0.00025, 0.0005, or 0.001 g is administered (0.25, 0.5 or 1 ml 0.1% solution). In severe poisoning with cholinomimetic or anticholinesterase substances 0.5—1 ml 0.1% solution is administered intravenously, if necessary the injection is repeated.

Maximal doses for adults (orally and subcutaneously): single — 0.001 g, daily — 0.003 g.

Maximal doses for children up to 6 months old: single — 0.0001 g daily — 0.0002 g; from 6 months to 2 years: single — 0.0002 g daily — 0.0004 g; 3—4 years: single — 0.00025 g daily — 0.0005 g; 5—6 years: single — 0.0003 g daily — 0.0006 g; 7—9 years: single — 0.0004 g daily — 0.0008 g; 10—14 years: single — 0.0005 g daily — 0.001 g.

In ocular practice 0.5—1% solutions (eye drops) are used. For therapeutic purposes 1—2 drops are administered 2—6 times daily. In severe cases an ointment containing 1% atropine is applied under the margin of the lids before retiring. Atropine is sometimes prescribed in combination with ethylmorphine in order to increase the effect.

¹ When using atropine in coronary insufficiency it is usually assumed that the vagus is the constrictor nerve for the coronary vessels and that when the transmission of impulses in the endings of the vagus is blocked by atropine this should lead to an increase in the blood flow through the coronary arteries. However, experimental investigations carried out recently by M. S. Vovsky and Y. B. Novikova show that atropine has no direct influence on the calibre of the coronary arteries and that the blood flow through them remains unchanged or is even reduced. Some increase in the blood flow was observed only when the pulse was accelerated. This evidently explains the inconsistent effect from atropine in angina pectoris.

When it is necessary to shorten the effect of atropine after its use for diagnostic purposes phosphacol is administered or physostigmine pilocarpine or amine

When using atropine one must be cautious in respect to the dosage and the possibility of heightened individual sensitivity must be borne in mind. A slight overdosage may cause dryness in the mouth, dilation of the pupils and palpitation. When instilling drops into the conjunctival sac, the region of the tear duct should be compressed to prevent the solution entering the nasolacrimal duct and being absorbed.

Atropine is contraindicated in glaucoma and marked organic changes in the cardiovascular system.

Available in powder form and in ampoules containing 1 ml 0.1% solution.

To be kept locked (List A) in well stoppered bottles or in sealed ampoules.

BELLADONNA PREPARATIONS
Belladonna, deadly nightshade (*Atropa Belladonna* L.) family Solanaceae. Grows in mountainous regions of the Crimea, Caucasus and Western Ukraine cultivated in various parts of the USSR.

Contains alkaloids of the atropine group (hyoscyamine, scopolamine, apoatropine, etc.). The alkaloid content in the leaves (*Folia Belladonnae*) ranges from 0.14 to 1.2% and in the roots from 0.4 to 1.3%. The USSR State Pharmacopoeia specifies an alkaloid content in the leaves of not less than 0.3% when the alkaloid content in the leaves is higher they are dispensed in a correspondingly smaller amount.

The pharmacological properties of belladonna correspond in the main with those of atropine.

Belladonna preparations (extracts and tinctures) are used as spasmolytics and analgetics in ulcer of the stomach and duodenum, cholecystitis, cholelithiasis and other diseases accompanied by spasms of the smooth muscles of the abdominal organs. They are likewise employed in bradycardia associated with hyperexcitation of the vagus nerve, etc.

Contraindicated in glaucoma and marked organic changes in the cardiovascular system.

Belladonna tincture (*Tinctura Belladonnae*) (List B). Transparent greenish brown liquid with characteristic odour and bitterish taste. Prepared from belladonna leaf and 40° alcohol contains 0.077–0.033% alkaloids.

Prescribed orally in doses of 5–10 drops.

Maximal doses for adults: single—0.5 ml (23 drops) daily—1.5 ml (70 drops).

Maximal doses for children: up to 6 months old: single—1 drop daily—3 drops; from 6 months to 1 year: single—1 drop daily—3 drops; 2 years: single—2 drops daily—6 drops; 3–6 years: single—3 drops daily—9 drops; 7–9 years: single—4 drops daily—12 drops; 10–14 years: single—4–6 drops daily—12–18 drops.

Dry belladonna extract (*Extractum Belladonnae siccum*) (List B). Brown or light brown powder with faint odour and characteristic taste. Contains from 14 to 16% alkaloids.

Thick belladonna extract (*Extractum Belladonnae spissum*) (List B). Thick brown mass gives a slightly turbid solution when mixed with water (1:10). Contains from 14 to 16% alkaloids.

Belladonna extracts are prescribed in the form of pills, mixtures, powders and suppositories in doses of 0.01–0.02 g.

Maximal doses of dry and thick extracts for adults: single—0.05 g daily—0.15 g.

Maximal doses for children: from 6 months to 1 year: single—0.0025 g daily—0.0075 g; 2 years: single—0.003 g daily—0.009 g; 3–4 years: single—0.004 g daily—0.012 g; 5–6 years: single—0.005 g daily—0.015 g; 7–9 years: single—0.0075 g daily—0.025 g; 10–14 years: single—0.01–

0.015 g daily — 0.03–0.015 g Infants up to 6 months old are not prescribed belladonna extracts

An infusion of belladonna root made with white wine and a dry extract of the root have been proposed for the treatment of parkinsonism, the latter is available in the form of tablets under the name «Corbella»

The following preparations containing powdered belladonna leaf and extracts of belladonna leaf and root are available

Corbella tablets (Tabulettae Corbella) Dry extract of belladonna root in the form of tablets each tablet contains 0.001 g alkaloids calculated as atropine. The use of the preparation in medical practice is mainly based on the central cholinolytic effect of the alkaloids contained, and on their ability to abate tremor and lower the muscular tone in affections of the subcortical formations

Employed in Parkinson's disease and parkinsonism associated with chronic epidemic encephalitis and atherosclerosis, and in chronic manganese poisoning and other intoxications. Treatment is begun with the administration of 1 tablet once a day before retiring, gradually increasing the dose until the optimal effect is obtained. In order to achieve a stable effect it is recommended that there should be lengthy administration of the maximal dose tolerated well by the patient

Treatment is contraindicated in cases of general emaciation, kidney disease, cardiovascular disease, cardiac decompensation, a marked tuberculous process and glaucoma. During treatment with the preparation complications associated with its atropine like action may appear such as dryness in the mouth, paresis of accommodation, vertigo etc. In cases of low tolerance the dosage should be reduced.

To be stored in a dry place, observing safety precautions (List B)

Belladonna root juice Sukradbel (Succus radicle Belladonnae, Sucradbel lum) Contains 0.13–0.15% total alkaloids

Used in parkinsonism beginning with a dose of 3 drops, 2–3 times daily. The dosage can be gradually increased but the single dose should not exceed 15 drops

Possible complications and contraindications are the same as for Corbella tablets

Available in 30 ml bottles

To be stored in a place protected from light observing safety precautions (List B)

Asthma powder (Pulvis antiasthmaticus) (List B) Asthmatol (Asthma tolum) Composition belladonna leaf — 2 parts henbane leaf — 1 part, thorn apple leaf — 6 parts sodium nitrate — 1 part water — 3 parts. Brownish green powder with characteristic odour. When ignited, burns slowly and smoothly without flame until only ash is left

Used in bronchial asthma half a teaspoonful is burned and the smoke inhaled

Available in packages of 50 g

Becarbon (Becarbonum) Composition belladonna extract — 0.01 g, sodium bicarbonate 0.3 g

Available in the form of tablets 6 to a packet

Besalol (Besalolum) Composition belladonna extract — 0.01 g salol — 0.3 g

Available in the form of tablets 6 to a packet

Bethiol, suppositories Composition belladonna extract — 0.015 g, ichthyol — 0.2 g, fatty base — 1.18 g

Used in hemorrhoid and fissures of the anus

Available in boxes of 10

Anusol (Anusolum) Composition belladonna extract — 0.02 g, bismuth tribromophenate — 0.1 g, zinc sulphate — 0.05 g, glycerine — 0.12 g, fatty base — 2 g. Suppositories

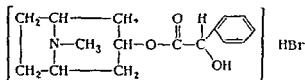
Used in hemorrhoid and fissures of the anus

Available in boxes of 10

Stomach tablets Composition a) belladonna extract—0.01 g basic bismuth nitrate—0.25 g salol—0.25 g b) belladonna extract—0.01 g basic bismuth nitrate 0.25 g c) belladonna extract—0.01 g wormwood extract—0.012 g valerian extract—0.015 g

SCOPOLAMINE HYDROBROMIDE (Scopolaminum hydrobromicum)

Hyoscine hydrobromide (Hyoscinum hydrobromicum) *Hyoscin hydrobromidum*



Hydrobromide of an alkaloid contained along with atropine in belladonna henbane thorn apple and scopolia

Colourless transparent crystals or fine crystalline powder freely soluble in water (1:3) soluble in alcohol (1:17) slightly soluble in chloroform Melting point 190—194° Solutions are sterilized by holding at 100° for 30 min Closely related chemically to atropine hydrobromide of the ester of scopolamine and tropic acid Similar to atropine in its influence on the peripheral cholinergic systems like atropine it causes dilation of the pupils paralysis of accommodation acceleration of the pulse relaxation of the smooth muscles and reduction of secretion by the digestive and sweat glands Unlike atropine scopolamine has a sedative effect on the central nervous system depresses respiration and diminishes motor activity may have a hypnotic effect

Used in psychiatry as a sedative in neurological practice for the treatment of parkinsonism in surgery along with analgetics (morphine oxycodone hydrochloride promedol) in preparing patients for anesthesia (see p 48) in ocular practice in the form of a 0.25% solution in iritis and iridocyclitis and as a substitute for atropine for dilating the pupil for diagnostic purposes also used sometimes as an antiemetic and sedative in seasickness and airsickness (Aeron tablets are more often subscribed for this purpose)

Contraindications for the use of scopolamine are the same as for atropine The extremely wide range in individual sensitivity to scopolamine must be taken into account quite frequently the usual doses cause excitement hallucinations and other side effects

Scopolamine is administered orally (usually in solutions) subcutaneously and locally (eye drops) Therapeutic doses 0.00025—0.0005 g (0.25—0.5 mg) or 0.5—1 ml 0.05% solution

Maximal doses for adults (orally and subcutaneously) single—0.0005 g daily—0.0015 g

Available in powder form and in ampoules containing 1 ml 0.05% solution

To be kept locked (List A) in well stoppered bottles of amber glass in a place protected from light

Aeron (Aeronum) Tablets containing 0.0001 g scopolamine camphorate and 0.0005 g hyoscyamine camphorate

The effect depends on the peculiarities of the pharmacodynamics of scopolamine and hyoscyamine which is more potent than atropine

Aeron tablets are used for the prevention and treatment of seasickness and airsickness and also for preventing or aborting attacks of Meniere's disease Sometimes used to reduce the secretion of mucus and saliva in plastic operations on the face and in operations on the upper respiratory passages In airsickness and seasickness the tablets are given orally as a prophylactic, 1—2 tablets 30—60 min before departure and subsequently if necessary another tablet in 6 hours If Aeron is not taken as a prophylactic 1—2 tablets are given

at the first symptoms of sickness (nausea vertigo and headache), after which 1 tablet is given twice a day

Maximal doses for adults single — 2 tablets daily — 4 tablets

Maximal doses for children 7—9 years old single — 1 tablet daily — 2 tablets, 10—14 years old, single — 1½ tablets, daily — 3 tablets Children up to 7 years old are not prescribed Aeron

In exceptional cases when there is persistent vomiting suppositories containing as much scopolamine camphorate and hyoscyamine as an Aeron tablet

In the Meniere symptom complex 1 Aeron tablet is prescribed 2—3 times a day In facial operations 2 tablets are administered 20—30 min before the operation during the first two days after the operation 1 tablet is administered twice a day

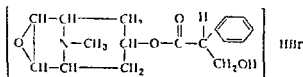
After taking Aeron thirst and dryness in the mouth and throat may be observed drink and caffeine are prescribed to relieve this condition The tablets must not be prescribed for patients with glaucoma

Available in glass tubes containing 10 tablets

Safety precautions must be observed during storage (List B)

HOMATROPINE HYDROBROMIDE (Homatropinum hydrobromicum Homatropini hydrobromidum)

Hydrobromide of the ester of tropine and mandelic acid



While crystalline powder odourless soluble in water (1 : 6) and in alcohol (1 : 40) Prepared synthetically

Closely related to atropine in chemical structure and pharmacological properties but less potent and has a less prolonged effect

Used in the form of a 0.5—1% aqueous solution for the most part in ocular practice as an agent causing dilation of the pupil and paralysis of accommodation Dilation of the pupil ensues quickly and passes away in 10—20 hours Contra indicated in glaucoma

Maximal doses for adults single — 0.001 g daily — 0.003 g

Available in powder form

To be kept locked (List A) in well stoppered bottles in a place protected from light

Rp Homatropini hydrobromici 0.1

Aq. destill. 100

MDS Eye drops

THORN APPLE LEAF (Folia Stramonii) (List B)

Dried leaves of the Thorn apple (*Datura stramonium* L.) of the Nightshade family (Solanaceae) Contain hyoscyamine and other alkaloids of the atropine group The alkaloid content should be at least 0.25% When the alkaloid content exceeds 0.25% a correspondingly smaller amount of the leaves is used Have an antispasmodic effect Ingredient of powders and cigarettes used in bronchial asthma (see Asthmafol)

Maximal doses for adults single — 0.2 g daily — 0.6 g

Asthmafol (Asthmatinum) A cigarette mixture used in bronchial asthma Contains 8 parts Thorn apple Leaf 2 parts Henbane Leaf and 1 part sodium nitrate

HENBANE LEAF (Folia Hyoscyami) (List B)

Dried rosette and stem leaves of Black Henbane (*Hyoscyamus niger*), family Solanaceae Contain 0.05% alkaloids of the atropine group (hyoscyamine, scopolamine and others)

The extract finds restricted application in the form of powders pills and mixtures as an antispasmodic and analgetic in place of Belladonna Extract (in doses of 0.02—0.05 g)

Maximal doses for adults single — 0.4 g, daily — 1.2 g

Ground Henbane Leaf is an ingredient of Asthmafin a cigarette mixture used in bronchial asthma (see Thorn apple)

Dry Henbane Extract (Extractum Hyoscyami siccum) (List B) Brown or light brown powder with characteristic odour Contains 0.3% alkaloids

Maximal doses for adults single — 0.1 g daily — 0.3 g

Thick Henbane Extract (Extractum Hyoscyami spissum) (List B) Thick brown extract Alkaloid content and maximal doses the same as for the dry extract

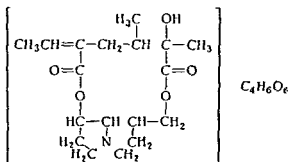
Henbane Oil Oil extract of Henbane (Oleum Hyoscyami) Obtained from Henbane Leaf by extraction with 95° alcohol and sunflowerseed oil in the presence of ammonium hydroxide The alcohol and ammonia are distilled off leaving a transparent oily liquid of green or brownish green colour and characteristic odour An ingredient of liniments (see Capsin Salniment p 54)

PLATYPHYLLINE (Platphyllinum)

Alkaloid contained in the Broad leaved Groundsel (Senecio platyphyllus DC.) family Compositae

Derivative of heliotridan (1 methyl pyrrolizidine)

In medical practice the bitartrate (hydrotartrate) of platyphylline (Platyphyllinum bitartaricum Platphyllinum hydrotartaricum) is used



White crystalline powder bitter taste freely soluble in water (1:5 in hot water and 1:10 in cold) practically insoluble in alcohol chloroform and ether Melting point 190—195° (decomp) Specific rotation in 5% solution = —38° —40° pH of 0.2% solution = 3.6—4.0 Solutions are sterilized by holding at 100° for 30 min

Similar to atropine in its influence on the peripheral cholinoreactive systems less active than atropine but when given in suitable doses the effect is not inferior to that of atropine Depresses the cholinoreactive systems of the autonomic ganglia to a greater extent than atropine Has a sedative effect on the central nervous system particularly the vasomotor centres also possesses a spasmolytic (papaverine like) action

Platyphylline is used as a cholinolytic and spasmolytic agent in spasms of the smooth muscles of the abdominal organs in ulcer of the stomach and duodenum and in bronchial asthma it has a favourable effect in spasms of the blood vessels (in hypertensive disease stenocardia and spasms of the cerebral vessels)

In ocular practice platyphylline is employed as a mydriatic its influence on accommodation is less marked than that of atropine The effect on the pupil is less prolonged than that from atropine and homatropine (paresis of accommodation from the administration of atropine lasts 6—7 days from homatropine — 10—20 hours and from platyphylline — 5—6 hours)

Platyphylline is prescribed in the following dosages to abort sharp pain from ulcer as well as intestinal hepatic and renal colic — 1–2 ml 0.2% solution subcutaneously. For systematic use platyphylline is prescribed orally in powders 0.003–0.005 g and in 0.5% solution, 10–15 drops 2–3 times a day or 1–2 ml of 0.2% solution may be administered subcutaneously. Platyphylline can also be prescribed in suppositories containing 0.01 g to be used twice a day or in microenemas of 20 drops of 0.5–1% solution 2–3 times a day. In ocular practice, a 1% solution is used for diagnostic purposes and a 2% solution for therapeutic purposes.

Maximal doses for adults (orally and subcutaneously) single — 0.01 g daily — 0.03 g

Maximal doses for children up to 6 months old single — 0.0001 g daily — 0.0012 g from 6 months to 1 year single — 0.0006 g daily — 0.0025 g 2 years single — 0.001 g daily — 0.003 g 3–4 years single — 0.0015 g daily — 0.0045 g 5–6 years single — 0.0025 g daily — 0.0075 g 7–9 years single — 0.003 g daily — 0.009 g 10–14 years, single — 0.005 g daily — 0.015 g

Side effects are usually not observed when platyphylline is administered in the doses indicated but overdosage may cause the same symptoms as overdosage of atropine (dryness in the mouth, palpitation, dilation of the pupils, etc.).

Platyphylline is contraindicated in glaucoma, marked organic changes in the cardiovascular system and organic diseases of the liver and kidneys.

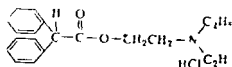
Available in powder form and in ampoules containing 1 ml 0.2% solution.

To be kept locked (List A) in tightly closed bottles or in sealed ampoules.

b) Synthetic substances (esters of carbonic acids)

SPASMOLYTIN (Spasmolytinum)

B Diethylaminoethyl diphenylacetate hydrochloride



Synonyms: Adiphenin, Diphacyl, Trasentin, Vagospasmyl

White crystalline powder, bitter taste, freely soluble in water. Stable when dry; aqueous solutions are slowly hydrolyzed.

Spasmolytin is a representative of a large group of new drugs which are esters of diphenylacetic acid and related carbonic acids (see Amizyl, Benzacin, Methacin, Mepanil, Apropren, Diprophren, Tiphren). These substances have cholinolytic, spasmolytic, and local anesthetic effects, as well as other pharmacological properties. In the individual compounds it is the peripheral m or n cholinolytic, the central cholinolytic, or the spasmolytic effect that is predominant depending on the chemical structure.

Spasmolytin possesses moderate peripheral m cholinolytic (atropine-like) activity besides which it has a blocking effect on the n cholinoreactive systems of the autonomic ganglia and the central nervous system. Spasmolytin has a pronounced spasmolytic effect: it relaxes the smooth muscles of the internal organs and the blood vessels. It also causes local anesthesia.

Spasmolytin is used in stenocardia, endarteritis, pylorospasm, spastic colitis, renal colic and ulcer of the stomach and duodenum, as well as in neuralgia, neuritis, and radiculitis.

Prescribed orally (preferably in capsules after meals) in a dosage of 0.1—0.25 g 2—4 times a day Course of treatment 2—4 weeks Also employed for segmentary block (intradermal) and to block the sympathetic ganglia (20—50 m of 0.5% solution)

The use of spasmolytin may give rise to vertigo headache a feeling of intoxication dryness in the mouth and pain in the epigastric region When administered per os anesthesia of the mucous membrane of the oral cavity may be observed A moderate irritation of the tissues may develop at the site of injections

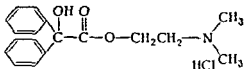
Available in powder form and in tablets of 0.1 and 0.25 g

To be stored in a dry place protected from light observing safety precautions

(List B)

BENZACIN (Benzacinum)

β Dimethylaminoethyl benzilate hydrochloride



Synonym Diphemin

White crystalline powder bitter taste freely soluble in water Melting point 184—186°

Closely related to spasmolytin in chemical structure and pharmacological properties differs from spasmolytin in having a hydroxyl group (OH) instead of a hydrogen atom at the carbon atom in the α position to the carboxyl group and in having methyl groups (CH₃) instead of ethyl (C₂H₅) attached to the nitrogen atom Differs from amizyl (see p 36) only in the presence of methyl groups instead of ethyl

Benzacin has a strong cholinolytic effect its influence on the cholinoreactive systems of the intestinal musculature is particularly marked In spasm of the intestine from the administration of acetylcholine or carbacholine (under experimental conditions) atropine is only twice as potent as benzacin Benzacin's influence on the bronchial musculature and the diameter of the pupil is less marked

The drug has a pronounced influence on the central nervous system it diminishes hyperkinesis caused by arecoline and potentiates hypnotics in which respect it is similar to amizyl It also has a spasmolytic effect acting directly on the smooth muscles

Benzacin is used as a spasmolytic in pain associated with spasms of the smooth muscles of the internal organs particularly spasms of the abdominal organs (spastic colitis cholecystitis renal colic ulcer of the stomach and duodenum etc.)

In neurosis the effect of benzacin is similar to that of amizyl

Benzacin is administered subcutaneously in a dosage of 0.0005—0.001 g (0.5—1 ml 0.1% solution) or orally in a dosage of 0.001—0.002 g 2—3 times a day

Maximal doses for adults single orally — 0.002 g subcutaneously — 0.001 g daily orally — 0.006 g subcutaneously — 0.003 g

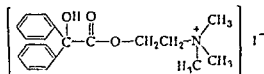
When benzacin is used the same side-effects may be observed as after the administration of atropine and other cholinolytic drugs dryness in the mouth acceleration of the pulse and dilation of the pupils as well as vertigo and a feeling of weakness in such cases the dose should be reduced The drug is contraindicated in glaucoma

Available in powder form and in tablets of 0.001 and 0.002 g

To be kept locked (List A) in a cool dry place

METHACIN (Methacinum)

Dimethylaminoethyl benzilate methiodide



White crystalline powder, bitter taste, sparingly soluble in water (1:200)
Melting point 191–195°

Methacin is a quaternary salt (methiodide) of benzacin. It has a considerably stronger influence on the peripheral m cholinoreactive systems than the latter. In its influence on the bronchial muscles methacin is several times more potent than atropine and in its influence on the intestinal muscles and on cardiac activity it is approximately equal to atropine. At the same time the mydriatic effect is only one tenth that of atropine. Being a quaternary compound methacin has little influence on the central nervous system.

Methacin is used as a cholinolytic and spasmolytic agent in diseases accompanied by spasms of the smooth muscle organs (bronchial asthma and spasms of the abdominal organs). In surgical practice methacin is employed in order to reduce salivation and secretion by the bronchial glands and also to prevent bronchial spasm and depression of the blood pressure which may ensue as a consequence of anesthesia and irritation of the branches of the vagus nerve. Methacin is more convenient for use in surgery than atropine because the mydriatic effect is weaker; this makes it possible to follow changes in the diameter of the pupil during the operation.

Methacin is administered orally (0.002–0.005 g 2–3 times a day), subcutaneously, intramuscularly or intravenously (0.0005–0.002 g = 0.5–2 ml 0.1% solution).

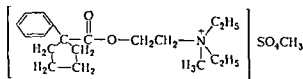
Possible side effects: tachycardia, dryness in the mouth and dilation of the pupils. Contraindicated in glaucoma.

Available in powder form in tablets of 0.002 and 0.003 g and in ampoules containing 1 ml 0.1% solution.

To be kept locked (List A) in amber containers in a place protected from light.

MEPANIT (Mepanitum)

Diethylaminoethyl phenylcyclopentanecarbonate methylsulfomethylate



Synonym: Merpanit

White crystalline powder, bitter taste, freely soluble in water (1:5). Melting point 71–72°

Mepanit is a quaternary salt of the diethylaminoethyl ester of phenylcyclopentanecarbonic acid which under the name of pentaphen (synonyms: Parpanit, Panparnit, Caramphen) was proposed as central cholinolytic agent for the treatment of parkinsonism. Mepanit has a stronger peripheral cholinolytic effect than pentaphen. In its m cholinolytic effect mepanit is only from one tenth to one fifth as potent as atropine, but it inhibits to a greater extent the transmission

of impulses in the autonomic ganglia, particularly the parasympathetic. In large doses it also blocks the sympathetic ganglia. The drug has no marked influence on the central nervous system.

Like other drugs of this type (see Benzacrin and Methacrin) mepanit is used in spasms of the smooth muscles of the internal organs (renal, hepatic and intestinal colic), ulcer of the stomach and duodenum, and bronchial asthma.

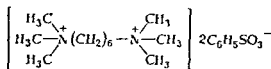
Mepanit is administered subcutaneously, it is not effective when given per os. The single dose is 0.02–0.03 g (1–1.5 ml 2% solution). If this is not sufficiently effective and the drug is tolerated well, the dose is increased to 0.04 g. The course of treatment is for 3–4 weeks. Possible side effects are the same as when methacrin is used. Mepanit is also contraindicated in glaucoma.

Available in powder form and in ampoules containing 2 ml 2% solution. To be kept locked (List A) in amber containers in a dry place.

D Ganglion-Blocking Agents

BENZOHEXONY (Benzohexonium)

1,6 Hexamethylene bis (trimethylammonium) dibenzylsulphonate



Synonyms Hexabenzat, Hexony B

White or creamy white, fine crystalline powder, faint characteristic odour, freely soluble in water, sparingly soluble in alcohol, insoluble in ether and acetone. Melting point 196–202° (over a range of 2°).

Quaternary bisammonium compound similar to the salts of tetraethylammonium in the character of its action but considerably more active, it is one of the most potent of modern ganglion blocking agents.

Other salts of 1,6 hexamethylene bis(trimethylammonium) can be used instead of the dibenzylsulphonate. The diiodide was formerly put out under the name of hexony. The diiodide and dibromide are put out abroad under the following names: Bistrium, Gangliostat, Hexamethonium, Hexameton, Hexanium, Hexathide, Hiohex, Methium, Methobromine, Methonium, Vegolysen, etc.

Benzohexony, like other drugs of this group, has the ability to block the cholinergic systems of the autonomic ganglia and inhibit the transmission of neural impulses from the preganglionic to the postganglionic fibres of the autonomic nerves. The autonomic ganglia also become only slightly sensitive to the excitatory action of various pharmacological stimulants (acetylcholine, nicotine, lobeline, cytisine, etc.). The drug's action extends to the sympathetic and parasympathetic ganglia. It also has an inhibitory influence on the carotid gland and the chromaffin tissue of the adrenals. In large doses benzohexony can also block the cholinergic receptors of the neuromuscular synapses and the central nervous system.

By interrupting the transmission of neural impulses through the autonomic ganglia, benzohexony alters the function of all organs having an autonomic innervation. Lowering of the arterial pressure is very marked, this is mainly due to the arrival of fewer vasoconstrictor impulses at the blood vessels and to the dilation of the peripheral vascular channel (particularly the arterioles), inhibition of the transmission of impulses arriving along the cholinergic (parasympathetic) nerves leads to impairment of accommodation, diminution of the motor and secretory activity of the organs of the gastrointestinal tract, diminution of glandular secretion, acceleration of the pulse and lowering of the tone of the bladder. The lowering of the vascular tone and depression of the carotid

gland and the chromaffinic tissue of the adrenals lead to a reduction of the secretion of adrenergic substances and the weakening of reflex pressor reactions

While chemically causing what might be called autonomic denervation benzohexony at the same time heightens the reactivity of the peripheral adrenergic and cholinergic systems the administration of adrenalin and acetylcholine has a stronger effect than before the use of the drug This pharmacological property is characteristic of many compounds which block the autonomic ganglia

Benzohexony is used in various diseases associated with impairment of neural regulation when reducing the number of neural impulses arriving at the organs can give a desirable therapeutic effect this includes spasms of the peripheral vessels (endarteritis intermittent lameness etc.) early stages of hypertensive disease (in the absence of organic changes in the cardiovascular system) hypertensive crises causalgia ulcer of the stomach, some forms of bronchial asthma hyperhidrosis etc

In surgery benzohexony is used like other ganglion blocking substances for so called "controlled" or artificially produced arterial hypotension i.e. for lowering the arterial pressure during the operation in order to diminish hemorrhage This method is extremely important for the prevention of hemorrhage in major operations involving a considerable loss of blood particularly craniocerebral operations The arterial hypotension caused by the drug leads to a sharp reduction in the flow of blood from the capillaries and small vessels and makes hemostasis much easier when the great vessels are injured In some cases the head of the operating table is raised to increase hypotension The effectiveness of this method is due to the fact that ganglion blocking substances depress the reflex mechanisms which maintain a constant level of arterial pressure when the position of the body is changed as a consequence the administration of such substances brings about "postural" hypotension the arterial pressure being lowered to the greatest extent when the patient is standing

The use of ganglion blocking substances for controlled hypotension should be carried out by an experienced physician and the necessary precautionary measures must be observed after the administration of the drug a careful watch must be kept on the arterial pressure (measurements every 5 min) pulse respiration and general condition of the patient It is considered that in artificial hypertension the arterial pressure should be 70—80 mm Hg and not lower than 50—60 mm If it is necessary to raise the arterial pressure a solution of mesaton can be slowly infused and the head of the operating table gradually lowered

The correct use of ganglion blocking agents usually lessens the danger of shock and eases the course of the postoperative period In cerebral operations there is less danger of edema of the brain

The use of ganglion blocking substances in anesthesia reduces the amount of anesthetic required

Benzohexony is administered subcutaneously and intramuscularly as well as per os for controlled hypotension it is administered intravenously Doses must be individualized taking into account the great variability in patients' reaction to the drug (just as to other ganglion blocking substances)

It must be borne in mind that on repeated administration the reaction to the drug gradually diminishes this requires an increase in the dose It is therefore recommended that treatment should be begun with the minimal dose that gives the necessary effect and then gradually increase the dose

For the treatment of vascular spasms hypertensive disease ulcer etc. it is recommended that the drug should at first be prescribed per os in a dose of 0.1 g 3—6 times a day If this dose is ineffective it is increased to 0.2 g or a shift is made to subcutaneous or intramuscular administration

For parenteral administration a 2% solution of benzohexony is used

The average therapeutic dose when the drug is administered subcutaneously or intramuscularly is 0.02—0.03 g daily (20—30 mg = 1—1.5 ml of 2% solution)

for adults The drug is given in a single injection or in two injections daily (each injection of 0.5—0.75 ml of 2% solution)

In surgical practice 0.015—0.020 g (15—25 mg) is administered intravenously at the beginning of the operation

Maximal doses of benzhexony for adults orally single — 0.3 g daily — 0.9 g subcutaneously single — 0.075 g daily — 0.3 g

Treatment with benzhexony is carried out in courses of 2—4 weeks with a break of 1—3 weeks between courses

When treating hypertensive disease it is expedient to combine the use of benzhexony (or other ganglion blocking substances) with the administration of apressine reserpine or other hypotensive agents

Caution must be observed when using benzhexony because of the possibility of side effects The most serious complication is orthostatic collapse In order to avoid this complication the patient must lie down before the drug is administered and for at least 2 hours afterwards

It is recommended that at the beginning of treatment the patient's reaction to small doses of the drug should be tested 10 mg should be administered and watch kept on the patient's condition It should be remembered that when the arterial pressure is elevated the hypotensive effect is more pronounced

After the administration of benzhexony the following side effects may be observed general weakness vertigo accelerated pulse dryness in the mouth dilation of the pupils and congestion of the vessels of the sclera These manifestations usually pass away of themselves

If there should be symptoms of collapse the patient's feet must be raised and small doses of mesaton ephedrine or nikethamide administered

When benzhexony is used for a lengthy period there may be atony of the intestine and bladder in this complication it is advisable to give carbacholine

Contraindications to the use of benzhexony hypotension marked atherosclerosis coronary insufficiency organic affections of the myocardium renal insufficiency and thrombosis as well as past history of myocardial infarction and cerebral hemorrhage Caution is necessary when prescribing benzhexony for the aged

A fact that must be taken into account is that the administration of benzhexony or other ganglion blocking substances causes dilation of the pupils which may lead to some narrowing of the canal of Schlemm and to a deterioration of the flow of liquid from the internal media of the eye An elevation of the intraocular pressure is however usually not observed on the contrary due to the lowering of the arterial pressure and the improvement in the outflow of lymph the intraocular pressure often falls

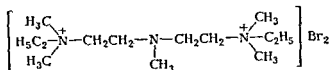
Treatment with benzhexony should be carried out on an inpatient basis

Available in powder form in tablets of 0.1 and 0.25 g and in ampoules containing 1 ml 2% solution

To be stored in a dry place protected from light observing safety precautions (List B)

AZAMETHONIUM BROMIDE (Azamethonium bromidum)

N N N', N 3 pentamethyl N N diethyl 3 azapentylene 1,5-diammonium dibromide (or pentamethyldiethylenetriamine dibromomethylate)



Synonyms Pentiomid Pentamethazene Pentamin

White crystalline powder hygroscopic freely soluble in water and alcohol Melting point 213—215° Aqueous solutions are sterilized by holding at 100° for 30 min pH of 5% solution = 6.0—7.5

Azamethonium bromide is closely related to benzohexony in chemical structure and pharmacological properties. It is a potent ganglion blocking drug.

Indications for the use of azamethonium bromide I and II stages of hypertensive disease, hypertensive crises, spasms of the peripheral vessels (intermittent lameness, endarteritis), spasms of the intestine and biliary tract, renal colic, retention of urine associated with cystitis and calculi in the bladder, bronchial asthma (for the abortion of acute attacks). It has been reported that azamethonium bromide is effective in eclampsia and causalgia.

In urological practice, azamethonium bromide is used in cystoscopy in the male in order to facilitate passage of the cystoscope through the urethra.

In surgery and neurosurgery, azamethonium bromide is used for "controlled hypotension".

When treating hypertension and other diseases, azamethonium bromide is administered intramuscularly. The dose must be individualized. In hypertensive disease, treatment is usually begun with a dose of 0.02 g (0.4 ml of 5% solution). If the drug is tolerated well, the dose is gradually increased to 0.1–0.15 g. Injections are given 2–3 times a day. Treatment is given in courses of 3–6 weeks. Treatment of hypertensive disease with azamethonium bromide can be combined with the prescription of a pressor or other hypertensive agents. In spasms of the vessels and other diseases, treatment is begun with a dose of 0.04 g, subsequently increasing the dose of 0.1 g 2–3 times a day.

The patient must be lying down before injections of azamethonium bromide and for at least 2 hours afterwards (in order to avoid orthostatic collapse).

Complications following the use of azamethonium bromide and contraindications are the same as for benzohexony. Treatment with azamethonium bromide should be on an inpatient basis.

For artificial arterial hypotension, a 2–5% solution of azamethonium bromide is slowly injected intravenously at the beginning of the operation. Men are usually given 50–60 mg and women 40–50 mg; if necessary, additional injections of 20–30 mg may be given during the operation (up to a total dose of 80–180 mg). Careful watch must be kept on the arterial pressure (measurements every 5 min).

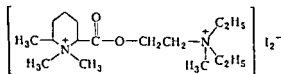
Available in ampoules containing 1 and 2 ml of 5% solution.

To be stored in a place protected from light, observing safety precautions.

(List B)

DICOLIN (Dicolinum)

Diethylaminoethyl 1,6-dimethylpipercolinate dimethiodide



White crystalline powder, freely soluble in water. Melting point 200–202° (decomp). Aqueous solutions are sterilized by holding at 100° for min.

Dicolin is a ganglion blocking agent. In the character of its action it is similar to benzohexony and azamethonium bromide but considerably more potent.

Dicolin is used in II and III stage hypertensive disease and in hypertensive crises, spasms of the peripheral vessels and abdominal organs, ulcer of the stomach and duodenum, attacks of bronchial asthma, etc.

Like other ganglion blocking drugs, dicolin causes an elevation of the tone and an intensification of uterine contractions. This effect is strongly manifested in dicolin and as a consequence it can be applied in obstetrics as an agent for stimulating labour, especially in women with nephropathy accompanied by

hypertension As a substance with a hypotensive effect it has an advantage in such cases over pituitrin and similar preparations Dicolin can also be used in treating late toxemia of pregnancy

Dicolin is administered orally, subcutaneously and intramuscularly

In hypertensive disease, treatment is begun with a dose of 0.05 g orally, the dose can subsequently be increased to 0.1–0.2 g (less frequently to 0.3 g) 2–3 times a day The course of treatment is for 3–6 weeks Intramuscularly or subcutaneously the initial dose is 0.01 g (1 ml 1% solution), gradually increasing the dose to 0.015, 0.02 or 0.03 g, 1–3 times a day When treating hypertensive disease, it is expedient to combine dicolin with reserpine, apressine or other hypotensive agents

In ulcer of the stomach and duodenum and in spasms of the peripheral vessels dicolin is prescribed orally in a dose of 0.1 g 2–3 times a day over a period of 2, 3 or 5 weeks In attacks of hepatic, intestinal or renal colic dicolin is prescribed orally in a dose of 0.1 g 2–3 times a day or subcutaneous or intramuscular injections are given (1–2 ml 1% solution), when the attack has ceased administration of the drug is continued orally for 1–2 days

For stimulating labour, dicolin is administered intramuscularly either in a single dose of 0.015–0.02 g (1.5–2 ml 1% solution) or at intervals of 1–1.5 hours Dicolin can be used in combination with other labour stimulating agents In late toxemia of pregnancy dicolin is administered intramuscularly in doses of 0.01 g 2–3 times a day over a period of 4–7 days

As a potent ganglion blocking agent dicolin can likewise be employed in surgical practice

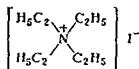
Contraindications, possible complications and measures for their prevention are the same as for benzohexony

Available in powder form in tablets of 0.05 and 0.1 g and in ampoules containing 1 and 2 ml of 1% solution

To be stored in a place protected from light observing safety precautions (List B)

TETAMON (Tetamonum)

Tetraethylammonium iodide



Synonyms Etamon Ethylon Etium Etylon Tetramon, Tetranum, Tetrylammonium

Transparent white crystals odourless, freely soluble in water (1:3), soluble in alcohol (1:35) Aqueous solutions are neutral to litmus Decomposition point 290°

The salts of tetraethylammonium were the first synthetic ganglion blocking drugs to find application in medical practice

Tetamon blocks the cholinergic systems of the autonomic ganglia, in which respect it is similar to benzohexony, azamethonium bromide and dicolin It is however much less potent and is used to only a limited extent today It is mainly employed for abating spasms of vessels in I and II stage endarteritis obliterans It is administered intramuscularly in the form of a 10% solution the dose for the first 2 days being 1 ml 2 ml is then given once a day for 4–6 weeks In cases of acute pain 2 ml are given twice a day for the first 10 days In order to avoid orthostatic hypotension the patient should be lying down during the injection and should be at rest before and after If a second course is required it should not be begun before the lapse of 3 months

Contraindications for the use of tetamon are the same as for benzohexony

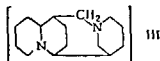
Available in ampoules containing 1 ml 10% solution

To be stored in sealed ampoules at room temperature in a place protected from light

PACHYCARPINE (*Pachycarpinum*)

Alkaloid contained in *Sophora pachycarpa* C. A. M., family Leguminosae also contained in *Thermopsis lanceolata* R. Br. and other plants

For medicinal purposes the hydroiodide of pachycarpine (*Pachycarpinum hydroiodicum*) is used



Pachycarpine hydroiodide: white crystalline powder, bitter taste, freely soluble in alcohol and chloroform, soluble in water (1:30), sparingly soluble in ether. Melting point 233–236°. Solutions for injection are sterilized by holding at 100° for 30 min. Solutions are stable and undergo no change on long standing. pH of 3% solution = 7.0–7.6.

Pachycarpine is a derivative of pyridine (lupinan group). Its structure is identical with that of sparteine, of which it is an optical isomer. Solutions of sparteine rotate the plane of polarization to the left; solutions of pachycarpine rotate it to the right.

Pachycarpine is a tertiary base; it does not contain the quaternary nitrogen atoms (the "onium" groups) characteristic of telamon, benzo-hexonyl, azamethonium bromide, and d. colin. Nevertheless, like those compounds, it has the ability to block the cholinergic systems. In this respect, pachycarpine is less active, but it is nevertheless convenient to use since it is easily absorbed when taken orally and has a marked effect when administered in this way.

Pachycarpine is chiefly employed as a ganglion blocking agent in hypertensive crises and spasms of the peripheral vessels (endarteritis and intermittent lameness). It is not recommended in hypertensive disease. It is also effective in ganglionitis. It has likewise been established that pachycarpine improves the function of the muscles in myopathy.

An important property of pachycarpine (as of some other ganglion blocking substances) is its ability to raise the tone and intensify uterine contractions. Because of this pharmacological property, pachycarpine is used to accelerate labour in cases of uterine inertia and early breaking of the waters, and also when bearing down efforts are weak. It can likewise be used instead of pituitary extract after the preliminary administration of castor oil and quinine, as well as after the preliminary administration of folliculin or synoestrol. The drug has advantages over pituitrin since it does not cause an elevation of the arterial pressure and can be prescribed for parturient women who are suffering from hypertensive disease.

Because of its tonic effect on the uterus, pachycarpine fosters a reduction in the loss of blood during the puerperal period.

Pachycarpine can be administered orally, subcutaneously, and intramuscularly.

In endarteritis obliterans, the drug is prescribed orally in a dose of 0.05–0.1 g 2–3 times a day. Treatment is for 3–6 weeks. If there is an exacerbation of the process, the course of treatment can be repeated in 2–3 months. In ganglionitis, pachycarpine is prescribed orally in a dose of 0.05–0.1 g twice a day for 10–15 days. In myopathy, the drug is given orally in a dose of 0.1 g twice a day for 40–50 days. The course of treatment can be repeated 2–3 times at intervals of 1–3 months.

When used to stimulate labour, pachycarpine is administered intramuscularly or subcutaneously in a dose of 3–5 ml of 3% solution (less frequently 0.1–0.15 g orally). Administration can be repeated in 1–2 hours. The stimulating

effect begins to be manifested in 15—30 minutes after administration. For greater effect, quinine can be given simultaneously in a dose of 0.2 g orally every 30 min (a total of 4 times). In cases of subinvolution of the uterus during the puerperal period pachycarpine is given orally in a dose of 0.1 g 2—3 times a day.

Maximal doses for adults single—0.2 g, daily—0.6 g

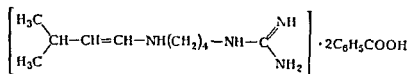
Pachycarpine is contraindicated in cases of impaired function of the liver or kidneys, stenocardia and marked cardiac disorders. Because of the stimulating effect on the uterine muscles, treatment with pachycarpine is contraindicated during pregnancy. The drug should only be dispensed on a physician's prescription.

Available in powder form, in tablets of 0.1 g and in ampoules containing 5 ml of 3% solution.

To be stored in bottles with ground glass stoppers in a place protected from light, observing safety precautions (List B).

SPHAEROPHYSINE (Sphaerophysinum)

Alkaloid isolated from *Sphaerophysa salsula* Pall DC., family Leguminosae, a plant native to Central Asia, Siberia and the Alta Territory. Available in the form of the benzoate (*Sphaerophysinum benzoicum*).



White, fine crystalline powder, odourless, bitter taste, freely soluble in water (1:2), in alcohol (1:35) and in solutions of caustic and carbonic alkalis; insoluble in ether and chloroform. Melting point 151—153°. Aqueous solutions are sterilized by holding at 100° for 30 min. Sphaerophysine has a blocking effect on the cholinergic systems of the autonomic ganglia and causes a lowering of the arterial pressure. Besides that, it raises the tone and intensifies uterine contractions.

Sphaerophysine is used as a hypotensive agent in I and II stage hypertensive disease. In obstetrics and gynecology it is employed in cases of uterine inertia, in postpartum hemorrhage and in atony of the uterus as an agent accelerating uterine retraction and promoting the cessation of hemorrhage; it can be used for parturient women who are suffering from hypertension and atherosclerosis in which case the administration of pituitary extract is impermissible.

Prescribed orally in powders and tablets in doses of 0.03 g, 2—3 times a day and also subcutaneously or intramuscularly in a dose of 1 ml 1% solution (also given 2—3 times a day).

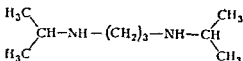
Maximal doses for adults — 0.05 g, daily — 0.1 g

Available in powder form.

To be stored in tightly closed bottles of amber glass, observing safety precautions (List B).

ISOPRINE (Isoprimum)

Diisopropylputrescine (diprine)



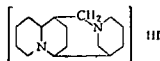
Colourless crystalline substance, bitter taste, freely soluble in water, sparingly soluble in alcohol. Melting point 279—279.5°.

To be stored in sealed ampoules at room temperature in a place protected from light

PACHYCARPINE (Pachycarpinum)

Alkaloid contained in *Sophora pachycarpa* C. A. M. family Leguminosae also contained in *Thermopsis lanceolata* R. Br. and other plants

For medicinal purposes the hydriodide of pachycarpine (Pachycarpinum hydriodicum) is used



Pachycarpine hydriodide white crystalline powder bitter taste freely soluble in alcohol and chloroform soluble in water (1:30) sparingly soluble in ether Melting point 233—236° Solutions for injection are sterilized by holding at 100° for 30 min. Solutions are stable and undergo no change on long standing pH of 3% solution = 7.0—7.6

Pachycarpine is a derivative of pyridine (lupin group). Its structure is identical with that of sparteine of which it is an optical isomer. Solutions of sparteine rotate the plane of polarization to the left solutions of pachycarpine rotate it to the right

Pachycarpine is a tertiary base. It does not contain the quaternary nitrogen atoms (the "onium" groups) characteristic of telamon, benzohexonyl, azamethonium bromide and dicolin nevertheless like those compounds it has the ability to block the cholinergic systems. In this respect pachycarpine is less active but it is nevertheless convenient to use since it is easily absorbed when taken orally and has a marked effect when administered in this way

Pachycarpine is chiefly employed as a ganglion blocking agent in hypertensive crises and spasms of the peripheral vessels (endarteritis and intermittent lameness). It is not recommended in hypertensive disease. It is also effective in ganglionitis. It has likewise been established that pachycarpine improves the function of the muscles in myopathy

An important property of pachycarpine (as of some other ganglion blocking substances) is its ability to raise the tone and intensify uterine contractions. Because of this pharmacological property pachycarpine is used to accelerate labour in cases of uterine inertia and early breaking of the waters and also when bearing down efforts are weak. It can likewise be used instead of pituitary extract after the preliminary administration of castor oil and quinine as well as after the preliminary administration of folliculin or synoestrol. The drug has advantages over pituitrin since it does not cause an elevation of the arterial pressure and can be prescribed for parturient women who are suffering from hypertensive disease

Because of its tonic effect on the uterus pachycarpine fosters a reduction in the loss of blood during the puerperal period

Pachycarpine can be administered orally subcutaneously and intramuscularly

In endarteritis obliterans the drug is prescribed orally in a dose of 0.05—0.1 g 2—3 times a day. Treatment is for 3—6 weeks. If there is an exacerbation of the process the course of treatment can be repeated in 2—3 months. In ganglionitis pachycarpine is prescribed orally in a dose of 0.05—0.1 g twice a day for 10—15 days. In myopathy the drug is given orally in a dose of 0.1 g twice a day for 40—50 days. The course of treatment can be repeated 2—3 times at intervals of 1—3 months

When used to stimulate labour pachycarpine is administered intramuscularly or subcutaneously in a dose of 3—5 ml of 3% solution (less frequently 0.1—0.15 g orally). Administration can be repeated in 1—2 hours. The stimulating

effect begins to be manifested in 15—30 minutes after administration. For greater effect, quinine can be given simultaneously in a dose of 0.2 g orally every 30 min (a total of 4 times). In cases of subinvolution of the uterus during the puerperal period pachycarpine is given orally in a dose of 0.1 g 2—3 times a day.

Maximal doses for adults single—0.2 g daily—0.6 g

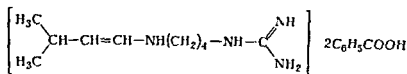
Pachycarpine is contraindicated in cases of impaired function of the liver or kidneys, stenocardia and marked cardiac disorders. Because of the stimulating effect on the uterine muscles treatment with pachycarpine is contraindicated during pregnancy. The drug should only be dispensed on a physician's prescription.

Available in powder form, in tablets of 0.1 g and in ampoules containing 5 ml of 3% solution.

To be stored in bottles with ground glass stoppers in a place protected from light, observing safety precautions (List B).

SPHAEROPHYSINE (Sphaerophysinum)

Alkaloid isolated from *Sphaerophysa salsula* Pall DC., family Leguminosae, a plant native to Central Asia, Siberia and the Alta Territory. Available in the form of the benzoate (Sphaerophysinum benzoicum).



White, fine crystalline powder, odourless, bitter taste, freely soluble in water (1:2), in alcohol (1:3.5) and in solutions of caustic and carbonic alkalis; insoluble in ether and chloroform. Melting point 151—153°. Aqueous solutions are sterilized by holding at 100° for 30 min. Sphaerophysine has a blocking effect on the cholinergic systems of the autonomic ganglia and causes a lowering of the arterial pressure. Besides that it raises the tone and intensifies uterine contractions.

Sphaerophysine is used as a hypotensive agent in I and II stage hypertensive disease. In obstetrics and gynecology it is employed in cases of uterine inertia, in postpartum hemorrhage and in atony of the uterus as an agent accelerating uterine retraction and promoting the cessation of hemorrhage; it can be used for parturient women who are suffering from hypertension and atherosclerosis, in which case the administration of pituitary extract is impermissible.

Prescribed orally in powders and tablets in doses of 0.03 g 2—3 times a day, and also subcutaneously or intramuscularly in a dose of 1 ml 1% solution (also given 2—3 times a day).

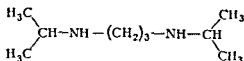
Maximal doses for adults — 0.05 g daily — 0.1 g

Available in powder form.

To be stored in tightly closed bottles of amber glass, observing safety precautions (List B).

ISOPRINE (Isoprimum)

Diosopropylputrescine (diprine)



Colourless crystalline substance, bitter taste, freely soluble in water, sparingly soluble in alcohol. Melting point 279—279.5°.

Isoprine is a synthetic compound, structurally it is closely related to spheroephysine and isoverine (see p 191) Has a ganglion blocking and hypotensive effect, also acts as a sedative

Used in the treatment of hypertensive disease (I and II stages), hypertensive crises, and spasms of the peripheral vessels Can be employed in surgical practice along with other drugs as an ingredient of "lytic mixtures" (see p 27), in obstetrics it is used in nephropathy of pregnancy and in psychiatry it is used in diseases accompanied by insomnia, headache and elevated arterial pressure

Prescribed orally or parenterally Orally it is given in a dosage of 0.025—0.05 g 2—3 times a day The course of treatment is for 7—10 days, the course can be repeated after a break of 10—15 days Subcutaneously, intramuscularly or intravenously 1—2 ml of 2% solution is administered

The same side effects are possible when taking isoprine as when taking other ganglion blocking drugs Constipation occurs relatively frequently, in order to avoid persistent constipation it is recommended that the administration of isoprine should be combined with administration of magnesium sulphate in doses of 1 tablespoonful of 10% solution

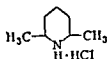
Contraindications are the same as for other ganglion blocking drugs

Available in powder form, in tablets of 0.05 g and in ampoules containing 2 ml of 2% solution

To be stored under ordinary conditions, observing safety precautions (List B)

NANOPHYN (Nanophynum)

2,6-Dimethylpiperidine hydrochloride



White crystalline powder freely soluble in water Melting point 279—281° Solutions are sterilized by holding at 100° for 30 min

Nanophyn is a synthetic substance — a secondary amine Has the ability to block the n cholinoreactive systems of the autonomic ganglia

The drug is used in treating I and II stage hypertensive disease Administered orally in doses of 0.1—0.2 g or subcutaneously and intramuscularly in a dosage of 0.02—0.05 g 2—3 times daily Treatment is in courses of 3—4 weeks Nanophyn is also effective in neurodermatitis and eczema

Contraindicated in marked atherosclerosis and impaired function of liver and kidneys

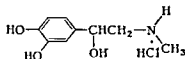
Available in powder form in tablets of 0.1 g and in ampoules containing 1 ml 2 and 5% solution

To be stored under ordinary conditions, observing safety precautions (List B)

E. Adrenalin and adrenomimetic agents

ADRENALIN (hydrochloride) (Adrenalinum hydrochloricum)

1 (3,4-dihydroxyphenyl) 2-methylaminoethanol hydrochloride



Synonyms Adrenallini hydrochloridum, Adnephryn, Adrenal, Adrenamine, Adrenine, Epinephran, Epinephrine, Epirenan, Hemisine, Hemostatine, Hypernephrin, Levorenine, Nephridine, Nieraline, Paranephrine, Renaglandin, Renaleptine, Renalina, Renosform, Renostypticin, Renostyptin, Styptirenal, Supradin, Supraneprhine, Suprarenalin, Suprarenine, Surrenine, Tokamina, Tonogen.

Adrenalin is obtained from the tissue of the adrenals of slaughtered cattle or prepared synthetically. Colourless or slightly pink crystalline substance. For medical purposes put out in the form of a 0.1% solution in 0.01 N hydrochloric acid, chlorobutanol being added as a preservative. The solution is a colourless or slightly yellowish transparent liquid of acid reaction $\text{pH} = 2.5-3.5$. On exposure to air and under the influence of light the solution is oxidized and assumes a pink colour. A slightly pink solution is permissible for use in medical practice. Brown solutions or solutions containing a precipitate are unfit for use. Solutions cannot be heated; they must be prepared in aseptic conditions.

Adrenalin is contained in the human and animal body; it is formed in the chromaffinic tissue, principally in the medullary layer of the adrenals.

According to contemporary conceptions adrenalin is a component of the mediator of the sympathetic (postganglionic) nerve fibres. The primary amine corresponding to adrenalin—noradrenalin (1 (3,4-dihydroxyphenyl) 2-amino ethanol)—is also a component of the mediator. The biochemical systems of the tissues of the body which react with adrenalin and noradrenalin are called adrenoreactive systems (or adrenoreceptors), while the sympathetic nerves for which these substances are mediators are called adrenergic nerves.

The action of adrenaline coincides, in the main, with the effects of stimulation of the sympathetic nerves. It causes a pronounced constriction of the vessels of the abdominal organs, skin and mucosa; to a lesser degree it constricts the vessels of the skeletal musculature and the brain, the coronary arteries and the pulmonary vessels, on the contrary, are dilated.

The arterial pressure rises under the influence of adrenalin.

Changes in cardiac activity are of a complicated character by stimulating the adrenoreactive systems of the heart, adrenalin promotes the strengthening and acceleration of cardiac contractions. Simultaneously, however, reflex changes resulting from the elevation of the arterial pressure cause a stimulation of the centre of the vagus nerves, which have an inhibitory influence on the heart. As a result cardiac activity may be retarded, when the centre of the vagus nerves is strongly stimulated arrhythmia may be observed. These side effects are abolished by atropine. When adrenalin is administered to patients with low arterial pressure, stimulation of the systems of the vagus is manifested to a lesser degree.

Adrenalin causes a relaxation of the muscles of the bronchi and intestine and dilation of the pupils (as a consequence of the contraction of the radial muscles of the iris which have an adrenergic innervation). Under the influence of adrenalin there is a rise in the sugar content in the blood and an intensification of tissue metabolism. Adrenalin improves the functional ability of the skeletal muscles (especially in a state of exhaustion), its action is also similar in this respect to the effect of stimulation of the sympathetic nerves (a phenomenon discovered by L. A. Orbeli and A. G. Ginetsinsky).

Adrenalin has a slight stimulating effect on the central nervous system.

Adrenalin is destroyed in the body by an enzyme, aminoxidase, which causes an oxidizing desamidization of the side chain.

Adrenalin hydrochloride is administered subcutaneously and intramuscularly; it is also applied locally (to the mucous membrane). It is at times administered intravenously (very slowly and cautiously). The drug is not prescribed internally since it is decomposed in the gastrointestinal tract.

Adrenalin is used in acute lowering of the arterial pressure (collapse), bronchial asthma, serum disease, and hypoglycemic coma (following an over

dose of insulin) In surgery it is employed to potentiate local anesthetics and reduce hemorrhage being added to the solution of the anesthetic immediately before use When used to stop hemorrhage it is applied locally on tampons In ocular and otolaryngological practice it is used in the form of drops and ointments

The therapeutic dose subcutaneously is 0.1–0.5 ml of 0.1% solution (less frequently up to 1 ml)

Maximal doses of 0.1% adrenalin solution subcutaneously for adults single—1 ml daily—5 ml

Maximal doses of 0.1% adrenalin solution subcutaneously for children up to 6 months old single—0.1 ml daily—0.3 ml from 6 months to 1 year single—0.15 ml daily—0.5 ml 2 years single—0.2 ml, daily—0.6 ml 3–4 years single—0.25 ml daily—0.75 ml 5–6 years single—0.3 ml daily—1 ml 7–9 years single—0.4 ml daily—1.5 ml 10–14 years single—0.6 ml daily—2 ml

Contraindicated in hypertension marked atherosclerosis thyrotoxicosis diabetes and pregnancy

Available in vials of 30 ml for local application and in ampoules containing 1 ml 0.1% solution for parenteral administration The potency is controlled by biological tests

To be stored in a cool place protected from light observing safety precautions (List B) Solutions can be stored for 1 year

ANTIASTHMOCRIN (Antiasthmocrinum)

Names of similar foreign preparations Adrenopituitin Asthmolysin Evalmin

Mixture of equal parts of 0.1% adrenalin hydrochloride solution and extract of the posterior lobe of the pituitary body (pituitrin) Transparent colourless or slightly yellowish liquid Possesses the pharmacological properties of adrenalin and pituitrin

Used in bronchial asthma as an agent aborting attacks Has a more prolonged effect than adrenalin

Administered subcutaneously at the beginning of or during attacks of bronchial asthma Adults are given 0.5–1 ml children up to 1 year—0.15–0.2 ml 2–5 years—0.2–0.3 ml 6–12 years—0.3–0.75 ml

Contraindicated in hypertension marked atherosclerosis diabetes and pregnancy

Available in ampoules containing 1 ml

To be stored in a cool dark place

Rp Antiasthmocrinum 10

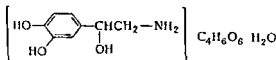
D t d N 6 in amp

S 1 ml subcutaneously — for an adult

0.3 ml subcutaneously — for a 7 year old child

NORADRENALIN (bitartrate) (Noradrenalinum bitartricum **Levarterenoli bitartras**)

1 (3,4 D hydroxyphenyl) 2 aminooethanol bitartrate



Synonyms Arterenol Levarterenol Levophed Norefol Norepinephrine Norexadrine Norlevorine

White or slightly greyish crystalline powder odourless soluble in water Darkens on exposure to light and air pH of solutions = 3.0–4.0

In its chemical structure noradrenalin differs from adrenalin in the absence of a methyl group attached to the nitrogen atom In its pharmacological pro

erties it differs from adrenalin in its greater vasoconstrictor and pressor effect, less stimulating influence on cardiac contractions, weak broncholytic effect, and weak influence on metabolism (absence of a pronounced hyperglycemic effect)

Noradrenalin has no stimulating action on the central nervous system

Used to raise the arterial pressure in cases of an acute fall as a consequence of surgical intervention, trauma or poisoning accompanied by depression of the vasomotor centres, etc., and also to stabilize the arterial pressure during operations involving the sympathetic nervous system. The use of noradrenalin does not take the place of blood transfusions or the administration of blood substitutes, it is only intended to raise the vascular tone

Noradrenalin is administered intravenously by the drip method. The noradrenalin solution is diluted with 5% glucose so that 1 l of glucose solution contains 4 ml 0.2% noradrenalin bitartrate (the equivalent of a 0.1% solution of the base). Infusion is at a rate of 0.25, 0.5 or 1 ml of the final solution per 10 kg of body weight per 1 min. The arterial pressure is carefully measured every 2 min, maintaining it at the necessary level

Subcutaneous injection of the solution must be guarded against because of the possibility of necrosis

The administration of noradrenalin is contraindicated in cyclopropane anesthesia because of the possibility of ventricular fibrillation. It should likewise not be used in complete atrioventricular block, atherosclerosis or hypertension

Acute bradycardia may develop under the influence of noradrenalin, it can be abolished by means of atropine

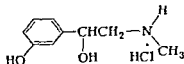
Only colourless or slightly yellowish solutions of noradrenalin should be used. The infusion of turbid or red solutions is impermissible

Available in ampoules containing 1 ml 0.1 and 0.2% solution

To be stored in a place protected from light, observing safety precautions

MESATON (Mesatonum)

1-(3-Hydroxyphenyl) 2-methylaminoethanol hydrochloride



Synonyms: Adrianol, Almetrin, Derizene, Idrianol, Isophrin, Neophryn, Neo Synephrine, Phenylephrine, in Sympatol, Visadron

White crystalline powder, odourless, freely soluble in water, dilute solutions of alkalis and alcohol. Melting point 142–146°. Solutions are sterilized by holding at 100° for 30 min

Mesaton is a synthetic drug, similar to adrenalin in the character of its effect: it causes a constriction of the peripheral blood vessels and an elevation of the blood pressure, dilation of the bronchi, inhibition of peristalsis of the intestine, and dilation of the pupils. It is less potent than adrenalin at equal doses but more stable. Can be sterilized and maintains its activity when administered orally. In the proper doses it has a strong and lasting effect

The drug is used: a) to raise the blood pressure in shock, collapse, hypotensive disease, loss of blood, intoxications, infectious diseases, in preparation for operations and in spinal anesthesia, b) to constrict the vessels and diminish inflammatory manifestations in vasomotor and allergic coryza, conjunctivitis, etc., c) as a substitute for adrenalin in solutions of anesthetics, d) to dilate the pupils

When used to raise the blood pressure: 0.3–1 ml 1% solution is administered subcutaneously or intramuscularly (for adults), intravenously, 0.1–0.3 ml

1% solution is given (inject slowly!), orally, administered in tablets or powders in doses of 0.01—0.025 g. For constricting the vessels of the mucosa and abating inflammatory manifestations, a 0.25—0.5% solution is applied locally or instilled. For local anesthesia, 0.3—0.5 ml 1% solution is added to each 10 ml of the anesthetic solution. For dilating the pupil, a 1% mesaton solution is instilled into the conjunctival sac.

Maximal doses for adults single — 0.03 g, daily — 0.1 g

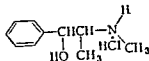
Mesaton is contraindicated in hypertensive disease, atherosclerosis and predisposition toward vascular spasms. Must be used with caution in diseases of the myocardium, in hyperthyroidism and in old age.

Available in powder form and in ampoules containing 1 ml 1% solution.

To be stored in tightly closed bottles of amber glass or in ampoules in a place protected from light, observing safety precautions (List B).

EPHEDRINE (hydrochloride) (*Ephedrinum hydrochloricum*)

1 Phenyl 2 methylaminopropanol hydrochloride



Synonyms: Ephedrosan, Ephelonin, Sanëdrine

Alkaloid contained in various species of Joint Firs (*Ephedra* L.), family Ephedraceae including the Horsetail *Ephedra* (*Ephedra equisetina* Bge.), found growing in the mountainous regions of Central Asia and Western Siberia, and *Ephedra monosperma* S. A. M. of the Trans-Baikal Territory, as well as others.

Ephedrine hydrochloride: fine colourless crystals or white crystalline powder, bitter taste, odourless, readily soluble in water (1:5), soluble in 95% alcohol (1:14), insoluble in ether.

Melting point 216—220°. Solutions are sterilized by holding at 100° for 30 min.

Natural ephedrine is levorotatory; specific rotation of 2.5% aqueous solution of hydrochloride = -33 — -36° . The synthetic product is racemic; it is similar in pharmacological properties to natural ephedrine but less potent.

Chemically, ephedrine is closely related to adrenalin; it differs from the latter in not having hydroxy groups in the aromatic cycle and in having amino-propanol rather than aminoethanol as a side chain.

In its pharmacological properties ephedrine is also closely related to adrenalin; it stimulates the adrenergic systems and causes constriction of the vessels, elevation of arterial pressure, dilation of the bronchi, inhibition of intestinal peristalsis, dilation of the pupils and an increase in the sugar content of the blood.

Ephedrine has a milder but considerably more prolonged effect than adrenalin. Because of its greater stability, ephedrine is effective when administered orally.

Ephedrine has a stimulating effect on the central nervous system and heightens the excitability of the respiratory centre. Has a stimulating effect in poisoning with narcotics and hypnotics. In this respect it is similar to phenamine and desoxyephedrine but the latter have a considerably stronger influence on the central nervous system.

The mode of action of ephedrine is also similar to that of phenamine; it lowers the activity of aminoxidase protecting adrenalin from enzymatic decomposition and fostering its reaction with the adrenergic systems but this apparently does not exhaust all its effects.

Ephedrine is used in acute lowering of the arterial pressure (in trauma operations and loss of blood) and in depression of arterial pressure accom-

panying infectious diseases as well as in hypotensive disease etc Employed in spinal anesthesia to prevent a fall in the arterial pressure Also used in bronchial asthma whooping cough hay fever, urticaria vasomotor coryza serum disease myasthenia seasickness and poisoning with narcotics and hypnotics

Ephedrine is administered orally subcutaneously intravenously and intramuscularly, the method depending on the indications In acute lowering of the arterial pressure slow intravenous administration is indicated in infectious diseases and before spinal anesthesia etc — subcutaneous injection in bronchial asthma — usually oral administration

Intravenously ephedrine is administered either at once or in the form of a lengthy drip infusion When injected at once ephedrine is given in a dose of 0.02–0.03 g (0.4–1 ml of 5% solution) By the drip method ephedrine is administered in isotonic saline in a total dose of 0.06–0.08 g The amount of isotonic saline ranges from 100 to 800 ml When administered subcutaneously the dosage is 0.02–0.05 g once or twice a day

In spinal anesthesia 1 ml of 5% ephedrine solution is injected subcutaneously 10–30 minutes before the beginning of anesthesia

Orally adults are prescribed 0.025–0.03 g 2–3 times a day children up to 1 year old — doses of 0.002–0.003 g from 2 to 5 years — 0.003–0.01 g from 6 to 12 years — 0.01–0.02 g

The course of ephedrine treatment usually lasts 10–15 days Ephedrine can also be prescribed in cycles of 3–4 days at three day intervals In bronchial asthma it is expedient to combine ephedrine with dimedrol aminophylline theobromine calcium gluconate tiphen or other spasmolytic agents Ephedrine is an ingredient of Theophedrine tablets which are used in bronchial asthma (see p. 170)

Maximal doses for adults when administered orally single — 0.05 g daily — 0.15 g subcutaneous administration single — 0.05 g daily — 0.1 g

Maximal doses for children up to 6 months old single — 0.0025 g daily — 0.0075 g from 6 months to 1 year single — 0.006 g daily — 0.02 g 2 years single — 0.008 g daily — 0.025 g 3–4 years single — 0.01 g daily — 0.03 g 5–6 years single — 0.012 g daily — 0.036 g 7–9 years single — 0.015 g daily — 0.045 g 10–14 years single — 0.015–0.025 g daily — 0.045–0.075 g

In most cases patients tolerate ephedrine well At times a slight tremor and palpitation are observed 15–30 min after administration but these symptoms quickly pass away Overdosage may cause a number of toxic manifestations nervous excitement insomnia trembling of the extremities retention of the urine vomiting sudoresis and rash

The drug is contraindicated in hypertension atherosclerosis severe organic heart disease and insomnia

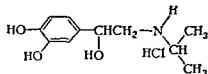
In order to avoid disturbed nocturnal sleep ephedrine and drugs containing ephedrine should not be prescribed before retiring or at the end of the day

Available in powder form in tablets of 0.025 g and in ampoules containing 1 ml 5% solution

To be stored in tightly closed bottles in a place protected from light observing safety precautions (List B)

ISADRIN (Isadrinum)

1 (3,4 Dihydroxyphenyl) 2 isopropylaminoethanol hydrochloride



Put out abroad in the form of the hydrochloride or sulphate under the following names Aleudrin Alidril Aludrin Antasthmin Asmanor Erydin Euspiran Iludrin Isodrenal Isonorin Isoprenalini hydrochloridum Isopropyl arterenol Isoproterenol Isorenin Isuprel Isupren Neodrenal Neocypine Neopinephrine Norisodrin Praedil, Propynalin Respiral Sanasma

White crystalline powder freely soluble in water Melting point 167—169° Aqueous solutions acquire a pink colour on exposure to light but there is no substantial change in the potency

In its structure and effect isadrin is closely related to adrenalin, it has a strong bronchodilator effect Unlike adrenalin the vasoconstrictor action is weakly manifested

Used to prevent or abort attacks of bronchial asthma and also in asthmoid and emphysematous bronchitis

Isadrin is prescribed in the form of a 0.5% aqueous solution for inhalation and in tablets containing 0.005 g of the drug to be held in the mouth until dissolved Inhalation is made by means of a pocket or other inhaler the dose for one inhalation is up to 1 ml Inhalations can be repeated 2—3 times a day if necessary A tablet or half a tablet is held in the mouth (under the tongue) without swallowing until it is completely dissolved

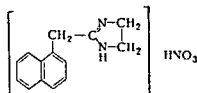
The drug gives a rapid effect Side effects are sometimes observed palpitation dryness in the mouth and a slight rise in the arterial pressure in such cases the dose must be reduced

Available in vials containing 10 and 25 ml of 0.5% solution and in tablets containing 0.005 g of the drug

To be stored in tightly closed containers of amber glass observing safety precautions (List B)

NAPHTHYZIN (Naphthyzinum)

2 Naphthyl 1 methylimidazoline nitrate



Synonyms Rinazina Sanorin

White crystalline powder with yellowish tint soluble in water (1 : 20) Melting point 169—170°

In its effect naphthyzin similar to the sympathomimetic amines stimulates the adrenoactive systems causes constriction of the peripheral blood vessels and elevation of the arterial pressure and dilates the pupils It has a considerably more prolonged vasoconstrictor effect than adrenalin and mesaton

Used as a topical vasoconstrictor in the treatment of acute and chronic rhinitis sinusitis and laryngitis in acute and chronic allergic conjunctivitis for stopping nosebleed Can also be employed to retard the absorption of local anaesthetics

Used in the form of a 0.025 0.05 or 0.1% solution for application to the mucosa or for instillation When applied to the nasal cavity 1—2 drops of 0.05—0.1% solution are instilled 2—3 times a day In nosebleed tampons moistened with 0.1% solution are used Applied to the conjunctival sac by instilling 1—2 drops of 0.05% solution In small children a 0.025% solution is used In infants caution must be observed sensitivity should first be tested by administering a single drop of 0.025% solution

When naphthyzin is used over a lengthy period of time there may be a weakening of the vasoconstrictor effect (the phenomenon of tachyphylaxis) in order to restore the effect a break of several days should be made in treatment.

In order to prolong the action of local anesthetics used for superficial anesthesia 2—4 drops of a 0.1% aqueous solution of naphthyzin is added per 1 ml of the anesthetic solution.

Naphthyzin is contraindicated in hypertension, tachycardia and marked atherosclerosis.

Available in powder form and in vials containing 10 ml of 0.05 and 0.1% solution.

To be stored in a place protected from light observing safety precautions (List B).

F Adrenolytic agents

The term adrenolytic agents¹ is applied to substances capable of blocking the adrenoreactive systems and weakening or even partially distorting the effects brought about by adrenalin. This action does not fully coincide with blocking of the neural impulses coming over the postganglionic sympathetic fibres since the adrenolytic substances known today only block the stimulating effects of adrenalin (constriction of the vessels, contraction of the radial muscle of the iris, etc.) while the inhibitory effects (for example the relaxation of the smooth muscles of the bronchi and the intestine) remain. Adrenalin's influence on the heart and its hyperglycemic effect are also only slightly altered. Since adrenolytic substances only block the adrenoreactive systems that receive vasoconstrictor impulses while the systems involved in the reception of inhibitory impulses (vasodilator sympathetic impulses) remain free, a distortion of the action of adrenalin is possible — a depressor effect may develop when adrenalin is administered.

It should be noted that it is much easier to block the effect of adrenalin with adrenolytic substances than it is to block the effect of noradrenalin — smaller doses are necessary and the result is more constant.

The principal contemporary adrenolytic agents that have been studied experimentally in detail belong to the following groups: a) the ergot alkaloids, b) the alkaloids of the yohimbine group, c) alkylamino derivatives of phenothiazine (chlorpromazine, etc.), d) benzodioxane derivatives and esters of phenyl alkylamines, e) derivatives of β -chloroethylamine (N (β -chloroethyl) dibenzylamine, sympatholitin, etc.), benzolin and its analogues.

In medical practice the drugs chiefly used besides chlorpromazine and its analogues are the hydrogenated derivatives of the ergot alkaloids.

The principal alkaloids of ergot are ergotamine, ergotoxine and ergometrine (syn. ergobasine, ergonovine). Ergotoxine itself consists of three alkaloids: ergocristine, ergocornine and ergocryptine. Ergotamine and the alkaloids of the ergotoxine group are peptide derivatives of lysergic acid. They have a powerful stimulating action on the uterine muscles and at the same time have an adrenolytic effect. They reduce the influence of adrenalin on the arterial pressure but the pressor effect is not completely abolished and a lowering of the arterial pressure does not take place since the alkaloids themselves have a strong vasoconstrictor effect associated with their direct influence on the walls of the vessels. Symptoms of ergotism observed in cases of poisoning with ergot are to be ascribed to prolonged tonic spasms of the vessels. Ergometrine (the hydroxypropylamide of lysergic acid) strongly stimulates the uterine muscles but has no marked adrenolytic action.

¹The term adrenolytic has been accepted in the literature. It must nevertheless be remembered that the substances in this group do not cause a change (lysis) of adrenalin. It would therefore be more correct to speak of them as adrenalin blocking or antiadrenalin agents.

the single course is for 2—4 weeks. It is recommended that at the end of the course treatment should not be ended abruptly but that the dose should gradually be reduced.

Treatment with apressine leads to a lowering of systolic and diastolic arterial pressure, abatement of headache and improvement in patient's general condition. After the course of treatment the hypotensive effect persists for 4—10 months or more. To lengthen the effect it is expedient to give repeat courses of treatment at intervals of 3—5 months (depending on the course of the disease). It is recommended that treatment should be given on an inpatient basis. Dosage and duration of treatment should be strictly individualized, taking into account the effectiveness of the drug and tolerance for it in individual cases.

Apressine treatment is often combined with the use of ganglion blocking drugs, reserpine and other hypotensive substances.

It has been reported that a combination of apressine and reserpine is particularly effective in eclampsia.

The following side effects are possible when apressine is used: headache, tachycardia, vertigo, pain in the region of the heart, rush of blood to the head, sudoresis, lacrimation, nausea, vomiting, erythematous rash, edema of localization and elevated temperature. Orthostatic collapse may also develop.

The manifestations enumerated are observed at the beginning of treatment with the drug; subsequently they usually disappear. If they are pronounced and persistent the dose should be reduced. In cases of nausea and vomiting that greatly disturb patients, antacid agents can be used. In many cases the side effects caused by apressine are abolished by dimedrol and other antihistamines.

At times headache following the administration of apressine can be aborted with caffeine.

Apressine is contraindicated in patients suffering from cardiac insufficiency, chronic kidney disease and sclerotic changes in the vessels of the brain and heart.

Available in powder form and in tablets of 0.01, 0.025 and 0.05 g.

To be stored in a cool, dry place, observing safety precautions (List B).

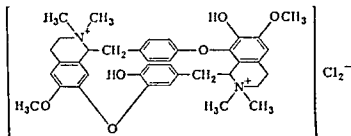
II. SUBSTANCES ACTING PREEMINENTLY IN THE REGION OF THE ENDINGS OF THE MOTOR NERVES (CURARELIKE DRUGS)

Curare and alkaloids and synthetic compounds used as substitutes for it are among the drugs that act preeminently in the region of the somatic neuromuscular synapses.

Curare is a mixture of the evaporated extracts of South American plants — species of *Strychnos* (*S. toxifera*, etc.) and *Chondodendron* (*Ch. tomentosum*, *Ch. platyphyllum*, etc.) — long used by the local population as arrow poisons.

When an animal is wounded with a poisoned arrow it loses the power of movement or dies as a result of asphyxia due to a stoppage of the contractions of the respiratory musculature. It was established as far back as the middle of last century that the paralysis caused by curare is a consequence of the stoppage of the transmission of impulses from the motor nerves to the muscles (Claude Bernard). Today this effect of curare is considered a consequence of the blocking of the cholinergic systems of the skeletal muscles. This deprives the latter of the ability to interact with acetylcholine, which is formed in the endings of the motor nerves and which is the mediator of the neural impulse.

In 1935 it was established that the chief active principle of "tube curare and of *Chondodendron tomentosum* is the alkaloid (+) — tubocurarine — a quaternary diammonium compound of ether character a derivative of bisbenzyl tetrahydroisoquinoline in which the optical distance between the onium groups (the quaternary nitrogen atoms) is about 15 \AA ¹



(+) Tubocurarine chiefly blocks the cholinoreactive systems of the skeletal musculature to a lesser extent it influences the cholinoreactive systems of the autonomic ganglia. In large doses it also blocks the cholinoreactive systems of the chromaffinic tissue of the adrenals and the carotid gland.

With small doses of (+) tubocurarine it is possible to achieve temporary relaxation of the skeletal muscles without significant changes in the basic functions of the body. When the dose is increased stoppage of respiration takes place; this is not dangerous if artificial respiration ("controlled respiration") is employed. In large doses asphyxia develops and death ensues.

(+) Tubocurarine has no marked direct influence on the cardiovascular system; however, doses which block the autonomic ganglia cause a noticeable lowering of the arterial pressure. In the usual doses (+) tubocurarine has no significant influence on the central nervous system but it potentiates the action of ether. A fact that must be taken into account is that (+) — tubocurarine promotes the liberation of histamine from the tissues and can cause spasm of the bronchial muscles.

(+) Tubocurarine has found application in medicine chiefly in surgery as a "relaxant" — an agent relaxing the skeletal muscles. When used in combination with nitrous oxide, barbiturates or ether it promotes a fuller relaxation of the muscles in this way facilitating the surgeon's work.

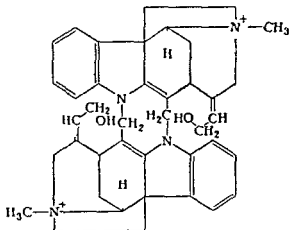
(+) Tubocurarine is likewise used at times in psychiatric practice to prevent traumatic injury during the convulsant therapy of schizophrenia (see Pen *lyleneletrazol* p. 69). It has not found extensive application in the treatment of spastic paralysis and prolonged convulsive states; this is mainly due to the transitory character of the effect and the difficulty of the method (the necessity of providing artificial respiration).

(+) Tubocurarine, like other quaternary ammonium salts, is absorbed poorly from the gastrointestinal tract and it is therefore administered parenterally for the most part intravenously. When injected intravenously the initial dose is 0.006–0.009 g (6–9 mg); if necessary an additional 3–4.5 mg is administered.

Recently new alkaloids which are considerably more potent than (+) tubocurarine have been isolated from "calabash curare" and various species of

¹ $\text{\AA} = 0.1 \text{ nm}$

Strychnos The most potent of these alkaloids and the one with the most prolonged and selective action is C toxiferine



When administered intravenously in a dose of 2 mg C toxiferine brings about relaxation lasting 50—160 min

Today various synthetic compounds (including diplacine paramylon and di tilin) and alkaloids are being used on a par with (+) tubocurarine as muscular relaxants

Different relaxants may have different modes of action due to the peculiarities of their influence on the process of synaptic transmission. According to present conceptions the excitatory wave on reaching the nerve endings causes the liberation of acetylcholine the latter interacts with the n cholinoreactive systems of the muscle fibres in this way bringing about the process of stimulation. As a result of local stimulation the synaptic zone becomes electronegative in respect to the neighbouring section. The resulting difference in potential creates a local current and the transmission of the excitatory wave along the muscle fibre. The effect of acetylcholine is characterized by a transitory act of contraction. The normal tone and contractions of the muscles are the result of the constant formation of acetylcholine and its rapid destruction by cholinesterase. In some pathological conditions and under experimental conditions (when anticholinesterase substances are administered) there may be an accumulation of superfluous acetylcholine in the region of the neuromuscular synapses. This causes the synaptic zones to be persistently electronegative and the process of muscular contraction is upset — after an initial abrupt contraction ("twitch") the muscle loses the ability to contract and gradually relaxes. As the acetylcholine is destroyed muscular contractions are again restored.

Muscular relaxants are divided into two groups according to the character of their influence on this process

a) drugs with a concurrent (hyperpolarizing) type of action ("pachycurares") among them are the alkaloids (+) tubocurarine C toxiferine etc. as well as synthetic curarelike substances that are concurrent antagonists of acetylcholine. They paralyze neuromuscular transmission by lowering the sensitivity of the n cholinoreactive systems of the synaptic region to acetylcholine in this way preventing the possibility of sufficient electronegativity being developed for the stimulation of the neighbouring section of the muscle fibre. The compounds in this group are genuine curarelike substances. Anticholinesterase substances are pharmacological antagonists of these compounds in the proper doses they lower the activity of cholinesterase in this way causing the accumulation of acetylcholine in the region of the synapses in high concentration the

latter weakens the reaction of the curarelike substances with the n cholinoreactive systems. Among the curarelike drugs of this group are diplacine paramylon etc.

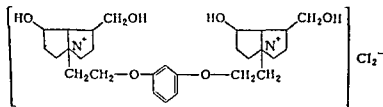
b) drugs with a depolarizing type of action ("leptocurare") these substances cause muscular relaxation by their persistent cholinomimetic effect i.e. they cause persistent electronegativity of the synaptic zones in the same way as superfluous amounts of acetylcholine. The drugs in this group are quite rapidly hydrolyzed by cholinesterase and a single administration has only a transitory effect. Anticholinesterase drugs potentiate their action. Diltin is a representative of this group.¹

(+) Tubocurarine, diplacine, paramylon and diltin are bisquaternary ammonium compounds—they are characterized by the presence of two "onium" groups. During the search for curarelike substances it was established that tertiary amines can also possess curarelike activity. Likely a number of alkaloids (delsamine, elatine, condelphine, etc.) have been isolated from various species of Larkspur (Delphinium), Buttercup family (Ranunculaceae), native to the USSR, which are tertiary bases but possess a marked curarelike effect.

a) Drugs with a concurrent type of action

DIPLACINE (Diplacium)

1,3-Di(β-platineciniummethoxy) benzene dichloride



Curarelike drug similar to (+) tubocurarine in its mode of action.

The administration of diplacine causes a characteristic curarelike effect manifested in transitory impairment of neuromuscular conductivity and relaxation of the skeletal muscles. When administered in small doses there may be relaxation of the skeletal muscles without stoppage of respiration. The weakening of respiration following large doses is due to impairment of the function of the respiratory muscles. When artificial respiration is resorted to the drug is tolerated in relatively large doses without the circulation being depressed. The paralyzing influence on neuromuscular conductivity is abolished by proserine and other anticholinesterase substances (eserine, galanthamine).

Diplacine is employed in surgery for the following purposes: a) to facilitate intubation during basal anesthesia with thiopental sodium;² b) for more complete relaxation of the muscles during operations on the abdominal organs (anesthesia with ether, nitrous oxides or barbiturates); c) for stopping independent breathing and employing "controlled respiration" during operations on the organs of the thoracic cavity.

When carrying out intubation diplacine is administered intravenously in a dose of 80–150 mg (4–7.5 ml of 2% solution on an average 1.5–2 mg per kg of body weight) mixed with 0.3–0.6 g thiopental sodium (2.5% solution). The mixture of drugs is infused slowly over a period of 2–3 minutes. Muscular relaxation sets in within 1–2 minutes after administration and the glottal

¹ It has lately been established that some curarelike drugs may have elements of two types of action (concurrent and depolarizing).

² If muscular relaxation is necessary only to facilitate intubation the use of diltin is preferable since its effect is transitory. In lengthy operations diplacine, paramylon and other drugs with a concurrent type of action are to be preferred.

chink opens making it easy to introduce the intubation tube into the trachea. General anesthetization with ether or nitrous oxide is then begun. In ether anesthesia in combination with diplocine the dosage of ether can be considerably reduced. The muscular relaxation that ensues after the initial administration of diplocine persists for about one hour. When it is necessary to prolong relaxation a second administration of diplocine can be given during the course of the operation (one half the initial dose) the total dose of diplocine during the entire operation can amount to 300–400 mg (15–20 ml of 2% solution). Children are given smaller doses of diplocine on the basis of their age and weight.

Maximal dose of 2% diplocine solution for adults (single and daily) — 25 ml

It must be borne in mind that the effect of diplocine is accentuated when the administration is repeated. In ether anesthesia the dose of diplocine should be reduced (by approximately one half). For complete stoppage of active respiration during operations on organs of the thoracic cavity "controlled respiration" being used instead diplocine must be given in large doses — at least 200 mg in a single administration for a body weight of 60–70 kg.

Diplocine causes an intense relaxation of the muscles. The use of diplocine in combination with nitrous oxide makes it possible to perform major operations without having recourse to ether or other anesthetics.

Information is also available on the use of diplocine to control convulsions in the combined treatment of tetanus (K. M. Loban).

In the proper dosage, diplocine is tolerated well by patients and causes no changes in the cardiovascular system.

Diplocine is only used in intubation anesthesia and when there are all the necessary facilities for artificial respiration. The intubation tube should be only removed after the restoration of sufficiently deep and regular independent breathing.

If it should be necessary to weaken the effect of diplocine proserine is administered intravenously. Atropine is given simultaneously with proserine (see p. 97). It must be remembered that when there is an overdosage of diplocine or other similar relaxants and when the dose of proserine is insufficient recarization is possible, i. e. there may be a subsequent relaxation of the muscles and stoppage of respiration. Treatment consists in the immediate intravenous administration of proserine and atropine along with artificial respiration. Diplocine is contraindicated in myasthenia, in impaired function of the liver or kidneys and in old age.

Available in ampoules containing 5 ml of 2% solution.

Diplocine solutions are to be stored in sealed ampoules in a place protected from light observing safety precautions (List B).

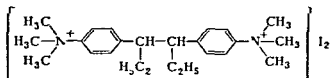
Rp Sol Diplocini 2% 50

D t d N 6 in amp

S For intravenous administration

PARAMYON (Paramyonium)

Meso-3,4 diphenylhexane bis p trimethylammonium diiodide



White crystalline powder freely soluble in hot water, soluble in cold water up to 0.5%. Melting point 226–229°

Paramyon is a synthetic curarelike drug. Administration causes temporary impairment of neuromuscular conductivity and relaxation of the skeletal muscles. When used in small doses there may be relaxation of the muscles without stoppage of respiration. Large doses also cause paralysis of the respiratory muscles and stoppage of respiration. In character and mode of action paramyon is similar to (+) tubocurarine and diplacine. Its paralyzing effect on neuromuscular conductivity is lessened by proserine.

Paramyon is employed in surgery for relaxing the muscles and also for stopping independent breathing in operations with "controlled respiration." Administered intravenously. To relax the muscles during anesthesia with nitrous oxide 3—4 ml 0.1% solution is given to stop active respiration 5, 7 or 10 ml of 0.1% solution is administered. In ether anesthesia the dose of paramyon is reduced for relaxing the muscles — 1.5—2 ml 0.1% solution for stopping respiration — 5 ml. After a single administration of the drug relaxation of the muscles persists for 30—60 min.

The use of paramyon like the use of diplacine makes it possible substantially to reduce the amount of ether consumed during an operation (up to 50%).

Paramyon like diplacine should only be used when all facilities for performing artificial respiration are at hand (see Diplacine).

Contraindications are the same as for diplacine. To be kept locked (List A).

DELSEMINE (Delsiminum)

Alkaloid contained in Central Asian species of Larkspur *Delphinium semibarbatum* Bienert *D. rotundifolium* etc.

Empirical formula $C_{27}H_{23}O_{10}N$ $\frac{1}{2}H_2O$ Tertiary base

White fine crystalline powder, odourless, bitter taste, slightly soluble in water (1:800), freely soluble in organic solvents. Melting point 120—125°.

Delsimine has a curarelike effect similar to (+) — tubocurarine in its mode of action on neuromuscular conductivity, has a stronger blocking influence on the n cholinoreactive systems of the autonomic ganglia and therefore causes a greater lowering of the arterial pressure. To lessen the hypotensive effect ephedrine hydrochloride is added to solutions of delsemine (acetate). Solutions are prepared according to the following formula: delsemine base — 5 parts, 1 N acetic acid — 7.2 parts, ephedrine hydrochloride — 0.1 part, twice distilled water — up to 100 parts. Solutions are Tyndallized and dispensed in ampoules of 2 and 5 ml.

Delsimine can be used as a relaxant in surgery.

The drug is administered intravenously at a rate of 0.5—2 mg per kg body weight. For the stoppage of independent breathing large doses are used (5—6 mg per kg body weight). The necessary amount of delsemine solution is made up to 10 ml with isotonic saline. In ether anesthesia smaller doses are required. The use of delsemine like the use of diplacine and paramyon makes it possible to reduce the amount of ether consumed during the operation. A "trial dose" of delsemine is first given ($\frac{1}{5}$ the total dose) and if there are no side effects the remainder is administered in 3—4 minutes. If necessary the administration of the drug is repeated (in a smaller dose).

Proserine is a pharmacological antagonist of delsemine in cases of an overdose of delsemine; it is administered intravenously along with atropine.

Delsimine should only be used when there are all facilities for artificial respiration (see Diplacine).

Contraindications for the use of delsemine are the same as for diplacine and paramyon; it should also not be administered to patients with decompensated cardiac activity.

Delsimine solutions are incompatible with solutions of barbiturates (cause precipitation).

To be kept locked (List A) in a place protected from light.

ELATINE (Elatinum)

Alkaloid contained in *Delphinium elatum* L. Empirical formula $C_{28}H_{25}O_{10}N_2$. Like delsemine a tertiary base.

White crystalline substance, sparingly soluble in water, freely soluble in organic solvents Melting point 220–223°

Elatine possesses curarelike properties, similar to tubocurarine in its mode of action on neuromuscular conductivity Effective not only when administered parenterally but also when given orally (in the proper doses) Also has a ganglion blocking effect and depresses the subcortical centres Lowers the arterial pressure somewhat Anticholinesterase drugs (proserine, galanthamine, etc.) are pharmacological antagonists of elatine in respect to neuromuscular transmission

Elatine is used for lowering the muscular tone and improving motor activity, for the most part in diseases accompanied by elevation of the muscular tone as a consequence of an affection of the pyramidal system Can also be used in vascular, traumatic and other lesions of the brain accompanied by hypertonia of the muscles, in traumatic, infectious and postoperative affections of the spinal cord, and in hyperkinesia Administration of elatine usually causes a reduction of spasticity, an abatement of pain in the extremities and an improvement in the general condition

Elatine is prescribed orally in powders or tablets in a dosage of 0.01 g 3–5 times a day The first two days patients are given one tablet a day if the drug is tolerated well, the dose is increased to 3–5 tablets a day The number of administrations per day and the duration of treatment depend on the effectiveness of the drug and the extent to which it is tolerated

The course of treatment is usually 20–30 days The therapeutic effect may set in within 1, 2 or up to 7 days and in some cases after the end of the course of treatment It is expedient to repeat the course of treatment in 2–3 months

If the indications are present, treatment with elatine should be combined with other methods of treatment and with therapeutic gymnastics

The use of elatine is contraindicated in myasthenia and other diseases accompanied by a lowering of the muscular tone, in impairment of the functions of liver or kidneys, as well as in decompensated cardiac activity

In the correct dosage elatine is tolerated without side effects In cases of heightened sensitivity to the drug or overdosage and the development of a feeling of extreme weakness and depressed respiration artificial respiration should be performed, oxygen given and 0.5–1 ml 0.05% proserine solution along with 0.5–1 ml 0.1% atropine solution slowly injected intravenously

Treatment must be carried out under the careful observation of a physician

Available in powder form and in tablets of 0.01 g

To be kept locked (List A) in a place protected from light

MELLICTINE (Mellitinum)

Hydroiodide of the alkaloid methyllicaconitine contained in various species of Larkspur (*Delphinium dictiocarpum* D *semibarbatum*, etc.) Empirical formula $C_{37}H_{50}O_{10}N_2$ Tertiary base

White crystalline powder, bitter taste sparingly soluble in water

Similar to elatine in pharmacological properties

Used for lowering the muscular tone in pyramidal insufficiency of vascular and inflammatory origin, postencephalitic parkinsonism and Parkinson's disease Little's disease, arachnoencephalitis and spinal arachnoiditis other diseases of pyramidal and extrapyramidal character accompanied by elevation of muscular tone and impairment of motor functions

Administered in doses of 0.02 g beginning with once a day and increasing to 5 times a day Course of treatment from 3 weeks to 2 months The course of treatment is repeated after a break of 3–4 months

To be kept locked (List A) in a place protected from light

CONDELPHINE (Condelphinum)

Alkaloid contained in *Delphinium confusum* M. Pop Empirical formula $C_{23}H_{35}O_6N$ Tertiary base

White or slightly yellowish fine crystalline powder practically insoluble in water freely soluble in alcohol and chloroform sparingly soluble in ether Melting point 130–134°

Condelphine has a curare like effect similar to (*) tubocurarine In its mode of action on the neuromuscular synapses In the proper doses effective not only parenterally but also when given orally Also has ganglion blocking effect lowers the arterial pressure somewhat and depresses the subcortical centres

The drug is used in the nervous diseases clinic in pathological elevation of the muscular tone and in other disorders of the motor function (hyperkinesia and constrained movement) associated with diseases of the central nervous system (parkinsonism diffused sclerosis spastic traumatic paralysis etc) Information is also available on the use of condelphine to control convulsions in the treatment of tetanus

Prescribed orally first day single dose of 0.025 g subsequently 0.025–0.05 g 1–3 times a day The single and daily doses as well as the duration of treatment should be individualized depending on the effectiveness of the drug and tolerance to it Course of treatment—10–12 days repeat courses are given if necessary

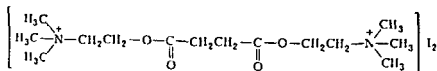
Contraindications and measures to be taken in cases of overdosage and heightened sensitivity are the same as for elatine Treatment must be carried out under the careful observation of a physician

To be kept locked (List A) in a place protected from light

b) Drugs with a depolarizing type of action

DITILIN (Ditilinum)

Dimethylaminoethyl succinate dimethiodide or dicholine succinate diiodide (diacetylcholine iodide)



Synonyms Brevitol M Celocaine Celosurin Curacholin Curacet Cura test Diacetylcholine Lysthenon Myo Relaxin Pantolax Succinolin (Corresponding chlorides Anectine Quelicin Scoline Succinylcholinum chloridum Succinyl Suxamethonium chloridum Suxinyl Syncuron)

White crystalline powder freely soluble in water sparingly soluble in alcohol and acetone Melting point 247–248° Aqueous solutions have a neutral reaction and are unchanged on sterilization

When administered intravenously impairs neuromuscular conductivity and causes relaxation of the skeletal muscles

Ditilin is easily destroyed by pseudocholinesterase being split into choline and succinic acid The drug has a rapid and transitory action has no cumulative effect For prolonged relaxation of the muscles repeated administration is necessary

Proserin and other anticholinesterase substances are not antagonists of ditilin on the contrary by inhibiting cholinesterase they prolong and heighten the effect

Ditilin's pharmacological properties make it possible to use the drug for patients with myasthenia

In the proper dosage ditilin is tolerated well and has no significant influence on the circulation At the moment of injection transitory convulsive contractions of the muscles may be observed these quickly give way to muscular relaxation

The principal indications for the use of ditilin are intubation, endoscopic procedures (broncho and esophagoscopy, cystoscopy, etc.), short operations (placing of sutures on the abdominal wall, reduction of fractures and luxations, etc.). In the proper dosage and when administration is repeated, ditilin can also be employed for longer operations. It has been reported that ditilin has been successfully used for preventing and allaying complications during convulsant therapy in psychiatric practice.

For transitory relaxation of the muscles ditilin is administered intravenously in a single dose of 15–25 ml 1% solution (for adults). The effect usually sets in within 30 sec., the duration depending on the dose and the patient's sensitivity. Maximal muscular relaxation (muscles of the pharynx, abdomen and extremities) is usually attained in 1–1½ min. and is maintained 3–7 min.

If it is necessary to achieve a prolonged effect, 2–25 ml 1% solution is administered intravenously, intubation is performed and drip infusion of ditilin begun at the same time going over to "controlled respiration." For drip infusion 0.5 g ditilin is dissolved in 250 or 500 ml of isotonic saline or 5% glucose solution (giving a 0.2 or 0.1% solution of ditilin) and administered at a rate of 40–60 drops (2–3 ml) per min.

Ditilin can be employed in various forms of anesthesia (with ether, nitrous oxide or thiopental). In all cases the administration of ditilin in large doses is permissible only after the patient has been put on "controlled respiration." When small doses are administered (1–1.5 ml) independent breathing can be maintained. Nevertheless in these cases, too, all the equipment necessary for artificial respiration must be ready for use.

Solutions of ditilin are incompatible with solutions of barbiturates (cause precipitation) and with blood (hydrolysis takes place).

Complications are ordinarily not observed when ditilin is used. After administration of the drug is discontinued the effect quickly passes away and the tone and contractive ability of the muscles and normal respiration are restored.

It must nevertheless be borne in mind that in individual cases there may be heightened sensitivity to ditilin and a more lengthy depression of respiration. It has been observed that such cases may occur, specifically, among patients suffering from diseases of the liver, this is apparently associated with impairment of the process of pseudocholinesterase formation.

When complications arise from the use of ditilin (prolonged depression of respiration) artificial respiration is resorted to and if necessary transfusions of plasma or blood are given.

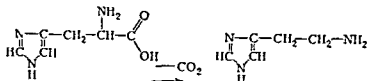
Available in powder form and in ampoules containing 2 ml of 1 and 2% solution.

To be kept locked (List A) in a cool dry place protected from light. Solutions in ampoules are fit for use over a period of 2 years.

Chapter III

ANTIHISTAMINE DRUGS

HISTAMINE or β imidazoleylethylamine is a biogenic amine formed by the decarboxylation of the amino acid histidine



Histamine is present in the animal and human body. Its physiological role has not as yet been studied sufficiently but there are grounds for considering that it is one of the chemical factors in the neuroreflex regulation of the vital functions. Under ordinary conditions histamine is present for the most part in the fixed inactive state. In some pathological processes (anaphylactic shock, burns and frostbite as well as hay fever, urticaria and other allergic diseases) and likewise when chemical substances are introduced into the body (including drugs e.g. tubocurarine etc.) the amount of free histamine increases substantially.

Free histamine is highly potent; it causes spasms of the smooth muscles (including the muscles of the bronchi), dilation of the capillaries and lowering of the arterial pressure. The sluggish flow of blood in the capillaries and the increased permeability of the capillary walls lead to edema of the surrounding tissues and thickening of the blood. The reflex stimulation of the medullary part of adrenals causes the secretion of adrenalin, the constriction of the arteries and the acceleration of the pulse. Histamine increases the secretion of gastric juice.

Histamine can be prepared by the bacteriological decomposition of histidine as well as synthetically.

Histamine is now employed to only a very limited extent as a medicinal agent. It is sometimes used: a) to determine the secretory ability of the gastric glands—in a healthy person the intramuscular injection of 0.5 mg histamine causes a considerable increase in secretion; the absence of a reaction gives grounds for assuming an organic change in the secretory system; b) in articular and muscular rheumatism and polyarthritis—the intradermal injection of 0.1–0.5 ml 0.1% histamine solution, the local application of an ointment containing histamine or iontophoresis with histamine cause pronounced hyperemia and the abatement of pain; c) in pain associated with an affection of the ner-

ves—in radiculitis plexitis etc. 0.2–0.3 ml 0.1% histamine solution is administered intradermally

The use of histamine requires great care. Overdosage and heightened sensitivity may lead to collapse and shock. As an antidote adrenalin is given (1 ml 0.1% solution) it is administered intramuscularly or if the condition is serious intravenously.

When administered by mouth histamine is absorbed poorly and does not give a constant effect.

Histamine is used extensively in pharmacology and physiology in experimental investigations. For this purpose the hydrochloride or phosphate is employed both are white crystalline hygroscopic powders freely soluble in water.

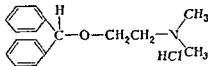
So called antihistamine drugs are now widely used in medical practice. These are substances that reduce the body's reaction to histamine they abolish the spasms of the smooth muscles caused by histamine lessen capillary permeability prevent the development of edema of the tissues reduce the hypotensive effect of histamine and prevent the development of allergic reactions or ease their course. Antihistamines sharply lower the toxicity of histamine.

Along with their antihistamine effect the drugs in this group also possess other pharmacological properties. Their antiphlogistic effect is very marked. Some of them (dimedrol, promethazine and fenethazine) have a sedative effect inhibit the transmission of neural impulses in the autonomic ganglia have a central cholinolytic action etc.

In medical practice antihistamines are chiefly employed in treating allergic diseases. They also be used in other pathological conditions the indications depending on the pharmacological properties of the individual drugs.

DIMEDROL (Dimedrolum)

B Dimethylaminoethyl benzhydryl ether hydrochloride



Synonyms: Alledryl, Allergan, "Bouty", Allergival, Am dryl, Benadryl, Benodine, Benzhydraminum, Dabylen, Desentol, Diabenyl, D bendrin, Dimedryl, Diphenhydramine, Diphenhydramini hydrochloridum, Restamin, Rigidil.

White fine crystalline powder, odourless, hygroscopic, freely soluble in water and alcohol, sparingly soluble in chloroform, almost insoluble in ether. Melting point 166–170°. Aqueous solutions are sterilized by holding at 100° for 30 min.

Dimedrol is one of the principal representatives of the group of antihistamine drugs. It is an extremely potent antihistamine. It also has other pharmacological properties: it has a local anesthetic effect, relaxes the smooth muscles as a result of its direct spasmolytic action and blocks the cholinergic reactive systems of the autonomic ganglia to a moderate degree.

Like other ganglion blocking agents, dimedrol heightens the excitability of the peripheral cholinergic and adrenoreactive systems.

Another important pharmacological property of dimedrol is its sedative effect, which is somewhat similar to that of neuroplegic substances (see p. 21). In some cases dimedrol has a hypnotic effect; it also has a moderate antiemetic action. When it comes to dimedrol's influence on the nervous system, its central cholinolytic effect is of considerable importance.

As a substance with antihistamine, antiallergic and antiphlogistic properties, dimedrol is chiefly used in the treatment of urticaria, hay fever, serum

disease hemorrhagic vasculitis (capillarotoxicosis) vasomotor coryza angio neurotic edema pruritic dermatosis acute iridocyclitis allergic conjunctivitis and other allergic diseases as well as allergic complications following the administration of diverse medicines including streptomycin and other antibiotics. It also abates side-effects caused by apressine.

Like other antihistamines dimedrol is employed in the treatment of radiation sickness.

Dimedrol has relatively little effect in bronchial asthma but it can be prescribed in this disease in combination with ephedrine aminophylline and other drugs. In some cases dimedrol is very effective in ulcer of the stomach and hyperacid gastritis.

Dimedrol can also be employed for lessening the reaction following the transfusion of blood and blood substitute liquids.

It has been reported that dimedrol is effective in parkinsonism chorea sea and airsickness vomiting of pregnancy and the Meniere syndrome. In these diseases the drug's therapeutic effect depends on its sedative and central cholinolytic action.

In some cases dimedrol can be used as a hypnotic (alone or in combination with other hypnotics).

Information is available on the use of a 10% dimedrol solution for local anesthesia in rhinological operations.

Dimedrol is also used as an ingredient of "lytic mixtures" (see p. 27). For this purpose however it is more expedient to use other antihistamines (promethazine or fenethazine) which have an adrenolytic effect.

Dimedrol is administered orally intramuscularly intravenously and locally (in the form of eye drops). It is not given subcutaneously because of its irritating effect. Orally it is taken in powders capsules or tablets in a dose of 0.03—0.05 g 1—3 times a day. The course of treatment is 10—15 days. Intramuscularly 0.01—0.05 g is administered in the form of 1—2% solution intravenously—0.02—0.05 g in 75—100 ml isotonic saline by the drip method.

Children are prescribed smaller doses of dimedrol: up to 1 year old—single doses of 0.002—0.005 g from 2 to 5 years—0.005—0.015 g from 6 to 12 years—0.015—0.03 g.

Maximal doses for adults: single—0.1 g daily—0.25 g.

Maximal doses for children: up to 6 months old: single—0.002 g daily—0.004 g from 6 months to 1 year: single—0.005 g daily—0.01 g 2 years: single—0.01 g daily—0.02 g 3—4 years: single—0.015 g daily—0.03 g 5—6 years old: single—0.02 g daily—0.04 g 7—9 years: single—0.025 g daily—0.05 g 10—14 years: single—0.03 g daily—0.06 g.

For instilling into the conjunctival sac a 0.2—0.5% solution is used (best prepared with 2% boric acid solution) in a dosage of 1—2 drops 2 to 5 times a day.

When dimedrol is taken orally there may be a transitory numbness of the mucous membrane of the oral cavity as a consequence of the local anesthetic effect. In rare cases vertigo headache dryness in the mouth and nausea may be observed. Side effects pass away of themselves when the drug is discontinued or the dose lowered.

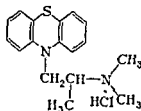
Drowsiness and general weakness may be observed as a result of the drug's influence on the central nervous system.

Because of dimedrol's sedative and hypnotic effect it must not be prescribed during working hours for drivers and other persons whose work requires a quick mental and motor reaction.

Available in powder form in tablets of 0.05 g and in ampoules containing 1 ml of 1% solution.

To be stored in tightly closed bottles of amber glass in a place protected from light observing safety measures (List B).

PROMETHAZINE (Promethazinum)
 10 (2'-Dimethylaminopropyl) phenothiazine hydrochloride



Synonyms Allergan, Atosil, Diprazine, Fargan Fenetazina, Phenergan Pipolphen, Proazamine chloride, Promazinamide, Promethazine, Promethazin hydrochloridum, Prothazin, Tamdil, VallerGINE

White or slightly yellowish powder, very freely soluble in water, freely soluble in alcohol and chloroform, insoluble in ether Melting point 221—225° The powder and aqueous solutions darken on exposure to light

Promethazine is a derivative of phenothiazine it is very similar to chlorpromazine in structure and somewhat similar in pharmacological properties (see also Diethazine and Fenethazine) The most important pharmacological property of promethazine is its strong antihistamine effect In this respect it is considerably more potent than chlorpromazine and is superior to dimedrol, being one of the most potent antihistamines used today At the same time it has a marked influence on the central nervous system it has quite a strong sedative effect, potentiates local and general anesthetics, lowers the body temperature and prevents or allays vomiting It also has a moderate peripheral and central cholinolytic action Promethazine's adrenolytic effect is very strongly manifested in this respect it is less potent than chlorpromazine but superior to fenethazine

Promethazine is chiefly used in the treatment of allergic diseases (urticaria serum disease, hay fever, etc), vasomotor and allergic rhinitis, rheumatism with a marked allergic component, allergic complications caused by penicillin, streptomycin and other drugs, pruritic dermatosis, Meniere's disease, chorea, encephalitis and other diseases of the central nervous system accompanied by heightened vascular permeability, sea and airsickness In surgery, promethazine is employed as one of the basic ingredients of lytic mixtures (see p 27) used for potentiated anesthesia and hypothermia and for preventing or abating postoperative complications during the operation and the postoperative period It is also employed for potentiating analgetics and local anesthetics

Promethazine is administered orally (after meals), intramuscularly and intravenously, it is not administered subcutaneously because of the irritating effect

Orally, adults are prescribed 0.025 g, 2—3 times a day, intramuscularly — 1—2 ml 2.5% solution, intravenously, as an ingredient of "lytic mixtures" — 5—10 ml 0.5% solution or 2 ml 2.5% solution

Maximal doses for adults single — 0.05 g, daily — 0.15 g

Children up to 6 years old are prescribed 0.008—0.01 g orally, 2—3 times a day, older children are prescribed 0.012—0.015 g, 2—3 times a day

Promethazine is usually tolerated well When taken orally it may cause moderate anesthesia of the mucous membrane of the oral cavity, at times dryness in the mouth and nausea develop When administered intramuscularly painful infiltrates sometimes form, and when administered intravenously a sharp lowering of the arterial pressure is observed at times Promethazine must be used with care in individuals with impaired function of liver and kidneys It must also be used with care in persons in a drunken state because of the intensification of the narcotic effect

Because of its sedative effect, promethazine (like dimedrol and fenethazine) should not be prescribed during working hours for drivers employed in transport, and people of similar occupations

Available in powder form, in tablets of 0.025 g and in ampoules containing 1 ml 2.5% solution and 5 ml 0.5% solution

To be stored in hermetically closed containers of amber glass, observing safety precautions (List B)

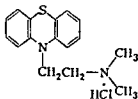
Note Promethazine has an irritating effect and may cause dermatitis and irritation of the mucous membrane. The same precautions must be observed when working with promethazine as when working with chlorpromazine

Rp Promethazini 0.025
D t d N G in tabul
S 1 tablet 2—3 times daily

Rp Sol Promethazini 2.5%, 10
D t d N G in amp
S 1 ml intramuscularly

FENETHAZINE (Fenethazinum)

10 (2' Dimethylaminoethyl) phenothiazine hydrochloride



Synonyms Anergan Etisine Liserгин Phenethazine

White crystalline powder, freely soluble in water. Melting point 218—224°. The powder and aqueous solutions darken on exposure to light.

Closely related in chemical structure to chlorpromazine, promethazine and diethazine. In pharmacological properties, fenethazine is closest to promethazine and possesses a pronounced antihistamine effect. In this respect it is more potent than chlorpromazine but somewhat inferior to promethazine. Like promethazine it also has a sedative effect; it potentiates local and general anesthetics and hypnotics; lowers the body temperature, and has an antiemetic effect. Nevertheless, in these pharmacological properties fenethazine is also somewhat inferior to promethazine.

Fenethazine possesses moderate adrenolytic and cholinolytic activity.

Indications for the use of fenethazine are the same as for promethazine. It is prescribed orally (after meals) intramuscularly and intravenously; it is not administered subcutaneously because of the irritating effect.

Fenethazine is usually prescribed orally for the treatment of allergic diseases, and diseases of the nervous system, etc. The dosage for adults is 0.025—0.05 g, 2—3 times a day. Children up to 7 years old are given doses of 0.01—0.12 g, those over 7 years old are given 0.015—0.025 g. The course of treatment ranges from 5 to 20 days or more, depending on the character of the disease. It has been reported that fenethazine is effective in the treatment of bronchial asthma in children when given in a dosage of 0.008—0.025 g, 2—3 times a day, over a period of 7—12 days (N. A. Turin).

For potentiated anesthesia, fenethazine is administered intramuscularly or intravenously in a dose of 0.025—0.05 g (5—10 ml 0.5% solution).

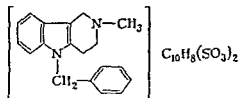
Possible complications and precautionary measures when administering fenethazine and when working with it are the same as for promethazine.

Available in powder form in tablets of 0.025 g and in ampoules containing 5 ml 0.5% solution

To be stored in hermetically closed containers of amber glass observing safety precautions (List B)

DIAZOLIN (Diazolinum)

N Methyl 9 benzyl 1,2,3,4 tetrahydrocarboline naphthalene 1,5 disulphonate



Synonyms Incidal Mebhydrolin Omeril

White fine crystalline powder, sparingly soluble in water and organic solvents

Diazolin is a potent antihistamine and has an antiallergic effect. Unlike dimedrol, promethazine and fenethazine, it has no sedative or hypnotic effect. This makes possible its use in cases where a depressing influence on the central nervous system is undesirable.

Diazolin is used in treating various allergic diseases: urticaria, serum disease, angioneurotic edema, hay fever, capillarotoxicosis, dermatitis, pruritus, allergic reactions arising from the administration of antibiotics, rheumatism with a marked allergic component, etc.

Diazolin is administered orally: adults 0.05–0.1 or 0.2 g once or twice a day; children — 0.02–0.05 g 1–3 times a day.

The drug is usually tolerated well. In order to avoid irritation of the mucous membrane of the stomach, it is recommended that diazolin should be taken after meals, preferably in capsules or sugar-coated tablets.

Contraindicated in ulcer of the stomach and duodenum and in inflammatory diseases of the gastrointestinal tract.

Available in powder form and in tablets of 0.05 and 0.1 g.

To be stored in a place protected from light, observing safety precautions (List B).

Chapter IV CARDIOVASCULAR AGENTS

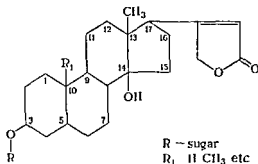
I HEART GLYCOSIDES

The principal medicinal agents having a selective action on the heart are preparations of plants which contain heart glycosides and the individual glycosides extracted from them

Plants containing heart glycosides include various species of Foxglove (*Digitalis purpurea* L. *D. lanata* Ehrh. etc.) species of Adonis (*Adonis vernalis* L. etc.) Lily of the Valley (*Convallaria majalis* L.) Silk vine (*Periploca graeca* L.) various species of *Erysimum* (*Erysimum canescens* Roth. *E. cheiranthoides* L. etc.) species of *Strophanthus* (*Strophanthus gratus* S. Kombe) Oleander (*Nerium oleander* L.) various species of Hellebore (*Helleborus purpurascens* W. et K. *H. niger* L.) etc.

All the heart glycosides are related chemically they are complicated organic compounds of the ether type which are hydrolyzed into a sugar and a non sugar component (aglycone or genin).

The aglycones have a complicated cyclopentanephenanthrene nucleus (with different radicals in the various glycosides) an unsaturated lactone ring being attached at position 17. (Scillaren A and scillaren B the glycosides of Squill—*Urginea maritima* and celerborin a Hellebore glycoside have a 6 membered ring instead of a 5 membered lactone ring)



The characteristic influence of these glycosides on the heart is chiefly associated with the aglycone present in their molecule. The sugars determine the

degree of solubility and permeability through the cellular membranes while themselves inactive they considerably potentiate the aglycones

Some of the heart glycosides have the same aglycone but differ in the sugar component others have the same sugar but different aglycones finally some glycosides differ from one another both in the sugar component and the aglycone The number of sugar units in the molecule ranges from one to four in some glycosides an acetic acid residue is joined to the sugar residue

Glycoside	Aglycone	Side chain
Digitoxin	Digitoxigenin	3 digitoxose residues
Digilanide A	»	3 digitoxose residues + 1 glucose residue + 1 acetic acid residue
Gitoxin	Gitoxigenin	3 digitoxose residues
Digilanide B	»	3 digitoxose residues + 1 glucose residue + 1 acetic acid residue
Oleandrin (Neriolin)	Oleandrogenin (16-acetylgitoxigenin)	1 oleandrose residue + 1 acetic acid residue
Digilanide C	Digoxigenin	3 digitoxose residues + 1 glucose residue + 1 acetic acid residue
Strophanthin K	Strophanthidin	1 cymarose residue + 1 glucose residue
Cymarin	»	1 cymarose residue
Convallatoxin	»	1 rhamnose residue
Convallaside	»	1 rhamnose residue + 1 glucose residue
Oritoride	»	Bovinoside + glucose
Erysimin	»	Digitoxose
Periplocin	Periplogenin	1 cymarose residue + 1 glucose residue

The various heart glycosides differ in the speed with which they are absorbed from the gastrointestinal tract as well as in the strength of the bond between them and the proteins of the plasma the rate at which they are excreted and the consequent diverse ability for cumulation and the degree of toxicity

All the heart glycosides are relatively slowly absorbed from the gastrointestinal tract and consequently when taken orally the less stable of them (the glycosides of Strophanthus Erysimum and Lily of the Valley) have a weak and unreliable effect on the heart Foxglove preparations thanks to the great stability of the glycosides have a pronounced therapeutic effect when taken by mouth

After absorption and entry into the blood the heart glycosides are fixed in the tissues including the myocardium The duration of the effect and the degree of cumulation depend on the rate at which the glycosides are excreted The

Foxglove glycosides particularly digitoxin have the most prolonged and cumulative effect strophanthin periplocin erysimin cymarlin and some other glycosides have a much lesser cumulative effect

The action of the heart glycosides is manifested in a change in all the basic functions of the heart The following changes take place under the influence of therapeutic doses

a) intensification of the systolic contractions of the heart the duration of the systole is shortened This effect is largely due to the direct influence on the heart

b) lengthening of the diastole the rhythm of the heart is retarded the diastole is lengthened and increased and the flow of blood to the ventricles is improved as a result of the simultaneous strengthening of the systolic contraction the working volume of the heart increases

The retarding of the rhythm is to a considerable degree due to the elevation of the tone of the centre of the vagus nerves It is not observed after atropinization The elevation of the tone of the centre of the vagus nerves is a reaction to the stimulation of the reflexogenic vascular zones which takes place when the pulse wave is strengthened as a result of the systolic action of the heart glycosides

c) lowering of the excitability of the transmission system of the heart conductivity through His bundle is retarded and the interval between the contractions of the atriums and the ventricles is increased (retarding of atrio-ventricular conductivity)

All these changes are manifested most constantly and distinctly in patients with impaired cardiac activity

The influence of the heart glycosides on the arterial pressure is not constant In congestive manifestations and lowered arterial pressure the latter rises as cardiac activity is improved in cases of elevated pressure marked changes are usually not observed The pressure in the peripheral veins ordinarily falls as circulation improves The vessels of the abdominal organs contract but the vessels of the kidneys dilate slightly The heart glycosides have no marked influence on the coronary vessels

Uresis increases under the influence of the heart glycosides this effect is largely due to the general improvement in circulation

Findings on the influence of the heart glycosides on the coagulability of the blood are contradictory it has been reported that the Foxglove glycosides increase coagulability but many authors consider these findings not sufficiently valid

The heart glycosides also have an influence on the central nervous system Adonis and Lily of the Valley preparations are often used in combination with bromides and Valerian as sedatives

In large doses the heart glycosides raise the excitability of the emetic centre This effect is largely reflex in character and is a consequence of the oral administration of glycosides which have an irritant action on the mucous membrane of the stomach It has been stated that the emetic effect is also associated with the reflexes which originate as a result of the stimulation of the cardiac receptors

When introduced into the subcutaneous cellular tissue solutions of the heart glycosides have an irritant effect

The influence of the different glycosides on the individual functions of the heart and on the body as a whole is marked by certain peculiarities Strophanthin for example has little influence on the frequency of cardiac contractions and does not perceptibly block His bundle the glycosides of the Woolly Foxglove increase uresis to a greater extent than other species of Foxglove Squill glycosides also have a relatively strong influence on uresis

In toxic doses the heart glycosides may cause nausea emesis and impairment of cardiac activity retarding of the pulse elevation of the blood pressure and dissociation between the atrium and ventricular rhythm — "atrioventricular

block" (as a consequence of blocking His's bundle) — followed by ventricular fibrillation and stoppage of the heart

Because of the ability for cumulation, the toxic effect may be manifested to a greater or less extent when heart glycosides are administered too long in the usual doses

The mode of action of the heart glycosides has not been fully explained. It has been established that they promote the normalization of carbohydrate metabolism in the myocardium, intensify the synthesis of glycogen from lactic acid and improve the utilization of oxygen (A. I. Cherkas)

They also improve the utilization of adenosine triphosphate by the myocardium. This promotes a fuller and more economical use of energy reserves by the decompensated myocardium and increases the productivity of its work

It must, however, be remembered that the heart glycosides themselves are not sources of energy. In cases of acute malnutrition of the myocardium they can cause the rapid exhaustion of the remaining energy stores by stimulating it to excessive activity

Consequently, when heart glycosides are used the patient's condition must be taken strictly into account, along with the correct choice of drug, the dosage, method and duration of administration etc. Treatment must be carried out under the careful observation of a physician

In order to ensure the correct dosage of heart glycosides preparations of definite potency must be used. Since in medical practice it is not only the pure glycosides that are used but plant preparations as well (powders, tinctures, etc.), which are not subject to exact chemical analysis these preparations are standardized by the biological method. According to the specifications of the USSR State Pharmacopoeia biological standardization is carried out on frogs and cats

In tests on frogs the unit of potency is defined as the minimal dose of the preparation causing the stoppage of the heart in systole in the majority of 5 frogs subject to test. This is one FUP (frog unit of potency). The sensitivity of the frogs to the given preparation on the day of the experiment is determined by simultaneously administering the corresponding standard preparation to five other frogs. One CUP (cat unit of potency) is the amount of the preparation causing stoppage of the heart when administered intravenously to an anesthetized cat (calculated for 1 kg body weight)

It must be borne in mind that the size of the therapeutic dose for different heart glycosides is determined not only by their biological potency, established by the methods described, but also by their stability in the body and their ability for cumulation when administration is repeated

A Foxglove preparations

Preparations of various species of Foxglove are being used today in medical practice: the Common or Purple Foxglove (*Digitalis purpurea* L.), the Woolly Foxglove (*D. lanata* Ehrh.), the Rusty Foxglove (*D. ferruginea* L.) and the Ciliated Foxglove (*D. ciliata*)

a) Purple Foxglove preparations

FOXGLOVE (PURPLE AND YELLOW)

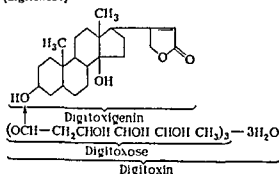
Purple or Common Foxglove (*Digitalis purpurea* L.) Figwort family (Scrophulariaceae) — perennial herb native to Western Europe, cultivated in the USSR. The USSR State Pharmacopoeia permits the use of another species on a par with the Purple Foxglove — the Yellow Foxglove (*Digitalis ambigua* Murr., *D. grandiflora* Lam.), grows in the European part of the USSR, in the North Caucasus and the Urals

In medical practice the dried leaf of both species and preparations made from it are used. The leaf contains glycosides, saponins and other substances

1 g leaf should contain not less than 50 and not more than 60 frog units. During storage, especially under unfavourable conditions, the potency of the leaf gradually declines.

Because of the possible loss of potency during storage all foxglove preparations are assayed biologically every year.

The leaves of the Purple Foxglove contain a number of "primary" (or "genine") glycosides (purpleaglycosides A and B, etc) which during drying and storage lose a molecule of sugar under the influence of enzymes, and are converted into "secondary" glycosides—the active principles of Foxglove preparations. Digitoxin and gitoxin—the most important of the secondary glycosides—consist of aglycones (digitoxigenin and gitoxigenin) and three sugar residues (digitoxose).



Digitoxin and gitoxin are sparingly soluble in water, unstable to acids and alkalis and decomposed by enzymes.

The glycosides of the Purple Foxglove, particularly digitoxin, are distinguished by their great stability in the body as compared with the other cardiac glycosides. Thanks to this they are fully effective when given by mouth. In spite of slow absorption from the gastrointestinal tract they gradually accumulate in the tissues and have a therapeutic effect. Their action usually develops in 8–12 hours after administration. They are slowly excreted and are characterized by a marked cumulative effect (this is especially true of digitoxin).

Indications for the use of Foxglove preparations: chronic cardiac insufficiency, insufficiency of the mitral valve (in a stage of decompensation), fluttering arrhythmia (small doses of Foxglove can change a tachycardiac form into a more favourable bradycardiac form) and other heart diseases.

The duration of Foxglove administration is determined by the length of time required for restoration of blood circulation and normal pulse, normalization of urysis, disappearance of edema and corresponding reduction in the patient's weight and improvement in sleep and the general condition. Ordinarily Foxglove preparations are prescribed for lengthy periods (several months).

During treatment careful watch must be kept on the cardiovascular system and the patient's general condition. When used properly there should be no side effects. The possibility of individual heightened sensitivity must be borne in mind.

The appearance of bradycardia or the isolated skipping of a beat as well as paired extrasystoles ("digitalis bigemina") requires the immediate withdrawal of the preparation so as to avoid complete atrioventricular block. Sometimes, after an overdosage of Foxglove, vomiting and decreased urysis are observed. In cases of toxic manifestations potassium chloride is indicated (see Potassium Chloride).

Foxglove is not indicated in compensated heart disease. Contraindications: coronary insufficiency (especially if there is sclerosis of the coronary vessels), myocardial infarction, impairment of conductivity (with the exception of cases

in which Foxglove is used specifically when it is necessary to bring about atrioventricular block in order to retard the contractions of the ventricles) paroxysmal ventricular tachycardia active endocarditis and rheumocarditis (danger of embolism)

Caution must be exercised when prescribing Foxglove preparations in aortic disease (particularly stenosis) accompanied by persistent bradycardia. In bradycardia which develops from small doses of Foxglove the latter can be prescribed along with Belladonna preparations.

Powdered Foxglove leaf and galenic preparations (*gitalen digipuren* etc.) are employed in medical practice. Lately individual crystalline glycosides (digitoxin and gitoxin) have also begun to be used.

Powdered Foxglove Leaf (*Pulvis foliorum Digitalis*) Pulverized leaves with petioles green powder. Potency 50–60 frog units in 1 g.

Prescribed orally for adults in doses of 0.05–0.1 g 2–3 times a day. Can also be prescribed in suppositories.

Children are prescribed the following doses: up to 1 year old—0.005–0.01 g from 2 to 5 years—0.02–0.03 g from 6 to 12 years—0.03–0.06 g.

Maximal doses for adults: single—0.1 g daily—0.5 g.

Maximal doses for children: up to 6 months old: single—0.005 g daily—0.02 g from 6 months to 1 year: single—0.01 g daily—0.04 g 2 years: single—0.02 g daily—0.08 g 3–4 years: single—0.03 g daily—0.12 g 5–6 years: single—0.04 g daily—0.16 g 7–9 years: single—0.05 g daily—0.2 g 10–14 years: single—0.05–0.075 g daily—0.2–0.3 g.

To be stored in small bottles of amber glass filled to the top, tightly closed and sealed with paraffin wax, observing safety precautions (List B). The potency of the powder is indicated on each bottle (the number of units in 1 g).

Available in powder form and in tablets of 0.05 g.

Foxglove Leaf Infusion (*Infusum foliorum Digitalis*) Prepared at the rate of 0.5–1 g leaf per 180 ml water. Adults are prescribed 1 tablespoonful 3–4 times a day. For children an infusion is made with 0.1–0.4 g leaf per 100 ml water; they are given from 1 teaspoonful to one dessertspoonful 3–4 times a day. The infusion can also be given in enemas.

Dry Foxglove Leaf Extract (*Extractum foliorum Digitalis siccum*) Powder containing a dry standardized extract of Purple Foxglove leaf mixed with lactose. 1 g of the extract is the equivalent of 0.25 g Foxglove leaf and contains 12.5–15 frog units.

Administered orally 1 tablet once or twice a day.

Available in powder form and tablets. One tablet contains 0.2 g dry extract, the equivalent of 0.05 g Powdered Foxglove leaf (up to 3 frog units).

To be stored in a dry place, observing safety precautions (List B).

Rp Pulv fol Digitalis 0.05

D t d N 12 (in tabul)

S 1 tablet 3 times a day

DIGITOXIN (*Digitoxinum*)

(See formula on p. 178)

Synonyms: Cardigin, Cardiotoxin, Cordalen, Cristapurat, Cristodigin, Digicin, Digipan, Digisidin, Digistrat, Digitin, Digitoxinol, Digitoxisidum, Digifrin, Digotin, Prodigat, Purodigin, Purpuren, Purpurat.

Colourless rectangular crystals of bitter taste, sparingly soluble in water, freely soluble in alcohol. Melting point 240–242°.

Digitoxin is the most potent of the Foxglove glycosides. It is almost completely absorbed from the gastrointestinal tract (the practical effect when given orally does not differ from the effect when given intravenously). It has a pronounced cumulative effect.

Doses of digitoxin and duration of treatment must be strictly individualized because of the cumulative properties, side effects characteristic of overdosage may develop relatively easily.

During the first few days digitoxin is prescribed in a dosage of 0.0003—0.0006 g (0.3—0.6 mg), 0.6 mg being given only if the patient has not received Foxglove preparations during the preceding fortnight.

The drug is prescribed in the form of tablets containing 0.0001 g (0.1 mg) of the glycoside, to be taken 3—6 times a day at intervals of 3—6 hours. In 3—5 days (depending on the effect) the dosage is reduced to 0.0001 g once or twice a day.

When the proper dosage is chosen the administration of digitoxin gives a marked therapeutic effect without side effects. If side effects develop (acute bradycardia, bigemina, pain in the region of the heart, nausea) the dose is reduced and if necessary administration of the drug is discontinued.

Available in tablets of 0.0001 g (0.1 mg)

To be kept locked (List A) in a dry place protected from light

GITOXIN (Gitoxinum)

Glycoside contained in the Purple Foxglove. In chemical structure differs from digitoxin in having an additional hydroxyl group (OH) in position 16 of the aglycone (see formulas on pp. 138—142).

White, fine crystalline powder, bitter taste, insoluble in water, sparingly soluble in alcohol. Melting point 263—265°.

Similar to digitoxin in pharmacological properties but less potent. For digitoxin, 0.42 mg is the equivalent of 1 cat. unit; for gitoxin, 1 mg is the equivalent of 1 cat. unit.

Like digitoxin, gitoxin is fully absorbed when taken orally, possesses marked cumulative properties.

Prescribed orally, beginning with a daily dose of 0.0003—0.0004 g (0.3—0.4 mg), the dosage being reduced subsequently to 0.0001—0.0002 g daily.

Possible complications and precautionary measures are the same as when using digitoxin.

Available in tablets of 0.0002 g (0.2 mg)

To be kept locked (List A) in a dry place, protected from light

GITALEN (Gitalenum)

Galenic preparation obtained from Purple Foxglove leaf, contains the total glycosides. Preserved by the addition of 20% alcohol.

1 ml gitalen contains 36 drops.

Transparent, colourless or slightly yellowish liquid of bitter taste and faint, characteristic odour. 1 ml contains 5 frog units, the equivalent of 0.1 g Foxglove leaf.

Prescribed orally, for the most part in chronic cardiac insufficiency, the dosage for adults being 10—15 drops, 2—3 times a day; children are given doses of 2—8 drops, depending on the age.

Maximal doses for adults, single—0.75 ml (27 drops), daily—1.5 ml (54 drops).

Maximal doses for children up to 6 months old, single—2 drops, daily—4 drops; from 6 months to 1 year, single—2 drops, daily—4 drops; 2 years, single—3 drops, daily—6 drops; 3—4 years, single—4 drops, daily—8 drops; 5—6 years, single—6 drops, daily—12 drops; 7—9 years, single—7 drops, daily—14 drops; 10—14 years, single—8—14 drops, daily—16—30 drops.

Available in vials containing 15 ml.

To be stored in a place protected from light, observing safety precautions (List B).

Preparations that have become turbid or yellow are not to be used.

Rp Gitaleni 150

DS 10—15 drops 3 times a day

(for an adult)

7 drops 2—3 times a day (for

a 9 year old child)

CORDIGIT (Cordigitum)

A preparation made from the dried leaves of Purple Foxglove, containing the total glycosides conventionally called "gitalin"¹

Slightly yellowish, amorphous, powder, sparingly soluble in water, freely soluble in chloroform, alcohol and acetone, insoluble in petroleum ether

Available in tablets containing 0.0008 g gitalin, the equivalent of 0.1 g standard Foxglove leaf

The cumulative effect of cordigit is less than that of digitoxin

Prescribed orally, $\frac{1}{2}$ —1 tablet, 2—4 times a day

To be stored in a place protected from light, observing safety precautions (List B)

Rp Tabul Cordigiti N 12

DS $\frac{1}{2}$ tablet twice a day

DIGIPUREN (Digipurenium)

Galenic preparation made from the leaves of Purple Foxglove and 70° alcohol, contains mostly digitoxin and gitalin 1 ml contains 9—12 frog units the equivalent of 0.2 g Foxglove leaf

Indications and contraindications are the same as for other Foxglove preparations

Administered orally, 10—15 drops, 2—3 times a day, may also be prescribed in the form of a micro enema

Available in vials containing 15 ml

To be stored in a place protected from light, observing safety precautions (List B)

Rp Digipureni 150

DS 10—15 drops 2—3 times a day
after meals

Rp Digipureni 150

DS 15 drops twice a day in
micro enema

DIGITASIDE (Digitasidum)

Galenic preparation containing the total glycosides of Purple Foxglove. Transparent liquid with characteristic odour, neutral or slightly acid reaction 1 ml contains 5 frog units the equivalent of 0.1 g Foxglove leaf

Administered intravenously when Foxglove preparations are indicated, particularly in serious impairment of the circulation requiring immediate intervention, and in cases when the patient cannot take Foxglove preparations orally

Administered intravenously, 0.5—1 ml once or twice a day, the preparation is injected slowly in 15—20 ml 20% (40%) glucose solution

Available in ampoules containing 1 ml

To be stored in a place protected from light, observing safety precautions (List B)

Rp Digitasidi 10

D t d N 6 in amp

S 0.5—1 ml intravenously
in 20 ml 20% glucose solution

b) Woolly Foxglove preparations

Woolly Foxglove (*Digitalis lanata* Ehrh) — perennial herb of the Figwort family (*Scrophulariaceae*), found growing in the wild state in the Balkan Peninsula, cultivated in the USSR

The active principles of the Woolly Foxglove are cardiac glycosides similar to the glycosides of the Purple Foxglove. The "primary glycosides contained in

¹ It was formerly assumed that gitalin was an individual glycoside consisting of the aglycone gitaligenin and two residues of the sugar digitoxose. Today it is considered that gitalin is a mixture of the glycosides digitoxin and d toxin

The effect is similar to that of alcoholic solutions of the total glycosides of Purple Foxglove but the preparation is absorbed more rapidly, it acts more quickly and has less cumulative effect

In some cases lantoside is more effective than Purple Foxglove preparations for example in patients with a congested liver

Prescribed orally 10—12 drops 2—3 times a day The length of treatment must be individualized depending on the patient's reaction and the course of the disease If necessary, lantoside can be administered in enemas (in a dose of 10 drops)

Maximal doses for adults single — 25 drops daily — 75 drops

The preparation is usually tolerated well but in individual cases side effects may be observed loss of appetite, nausea and vomiting In such cases the dose is lowered a break is made in treatment or a different preparation prescribed

Available in vials of amber glass containing 15 ml

To be stored in a cool place protected from light observing safety precautions (List B)

Rp Lantosidi 150

DS 10—20 drops 2—3 times a day

Rp Lantosidi 150

DS In enema 10 drops twice a day

DILANISIDE (Dilanisidum)

Galenic preparation containing 20% alcoholic solution of the total glycosides of Woolly Foxglove

Transparent slightly yellowish liquid bitter taste characteristic odour pH=4.4—5.5

1 ml contains 7—9 frog units the equivalent in potency of approximately 0.16 g Foxglove leaf Administered intravenously Has a relatively rapid effect The dose for adults is 0.5—1 ml Injected in 20 ml 20% (40%) glucose solution once or twice a day Injected slowly

Maximal doses for adults (intravenously) single — 1 ml, daily — 2 ml

Available in ampoules containing 1 ml

To be stored in a place protected from light observing safety precautions (List B)

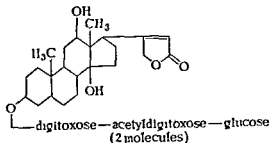
Rp Dilanisidi 10

D t d N 6 in amp

S 0.5—1 ml intravenously in 20 ml 40% glucose solution

CELANIDE (Cefanidum)

Primary (genuine) glycoside — lanatoside (or diglanide) C — from the leaves of Woolly Foxglove



Synonyms Cedilanid, Cedisanol Cedistabil Celadigal, Cristilanat C, Digilanid C Isolanid Lanacrist, Lano C

White powder, insoluble in water, soluble in methanol, sparingly soluble in ethanol slightly soluble in chloroform

Digilanide C acts on the heart in a way similar to that of the other Foxglove glycosides, the effect, however, is rapid, and there is relatively little cumulation in the body. It is very potent when taken orally, when administered intravenously acts almost as rapidly as strophanthin. Has relatively little influence on the system of the vagus nerve. The biological potency of the glycoside is about 16 000 frog units per g.

Used in cardiac insufficiency, atrial fibrillation and paroxysmal tachycardia. The preparation is administered intravenously or orally, depending on the indications. Intravenously, the dose is 1—2 ml 0.02% solution (0.2—0.4 mg) daily. Orally 1 tablet (0.25 mg) is given 2—3 times a day. Treatment is continued until cardiac activity and uresis are normalized. When a therapeutic effect has been achieved the dose is lowered.

Contraindications are the same as for other Foxglove preparations. Heightened individual sensitivity to the preparation must be taken into account (nausea, vomiting and loss of appetite).

Available in tablets of 0.00025 g (0.25 mg) and ampoules containing 1 ml 0.02% solution (1.6 000).

To be kept locked (List A)

Rp Celanidi 0.00025
D t d N 20 in tabul
S 1 tablet twice a day

Rp Sol Celanidi 0.02% 10
D t d N 6 in amp
S 1 ml intravenously in 20 ml
20% glucose solution

ABICIN (Abicinum)

Total genuine glycosides (digilanide A, B and C) from leaves of Woolly Foxglove

Synonyms Neodigan, Pandigal

White crystalline powder insoluble in water, soluble in methanol. 1 g contains approximately 16 000 frog units.

Indications, contraindications and dosage are the same as for celanide.

c) Rusty Foxglove preparations

Rusty Foxglove (*Digitalis ferruginea* L.) Figwort family (Scrophulariaceae), habitat—the Caucasus. The fresh leaves contain the "primary" glycosides digilanide A and digilanide B, as well as others.

In their pharmacological properties, indications and contraindications Rusty Foxglove preparations are similar to those of Purple Foxglove.

DIGALEN NEO

Water extract of leaves of the Rusty Foxglove, freed of inactive substances. Transparent, slightly yellowish liquid of bitter taste, neutral reaction.

Digalen neo for injections is preserved with 20% 96° alcohol. Digalen neo for oral administration is preserved with the same amount of alcohol and 0.3% chlorobutanol.

The effect on the cardiovascular system is that characteristic of Foxglove preparations.

Administered subcutaneously and orally, 1 ml of digalen neo for subcutaneous administration contains 3 frog units. 1 ml of the preparation for oral use contains 6 frog units, the equivalent in potency of 0.1—0.12 Foxglove leaf.

Used in disordered cardiac compensation and edema arising from impairment of cardiac activity, etc

Subcutaneously, adults are given injections of 0.5—1 ml once or twice a day Children up to 1 year old are given 0.05—0.1 ml, from 2 to 5 years—0.25—0.4 ml, from 6 to 12 years—0.4—0.75 ml

Orally, the dose is 5, 10 or 15 drops, 2—3 times a day

Maximal doses subcutaneously, for adults single—1 ml, daily—3 ml Maximal doses, orally, for adults single—20 drops daily—60 drops

Available in ampoules of 1 ml for subcutaneous injections and in vials of 15 ml for oral use

To be stored in a place protected from light observing safety precautions (List B)

Rp Digalen neo 10
D t d N 6 in amp
S 1 ml subcutaneously once a day

Rp Digalen neo 150
DS Orally, 10—15 drops 2—3 times
a day (for an adult)

SATITURANI

Preparation containing the total glycosides of the Rusty Foxglove Tablets contain 3 frog units Prescribed in dosage of 1 tablet, 2—3 times a day

Juice from leaves of Rusty Foxglove (*Succus foliorum Digitalis ferrugineae*), Succudifer

Juice from fresh leaves of Rusty Foxglove partially freed of inactive substances Preserved with 15% 96° ethanol and 0.3% chlorobutanol 1 ml contains 5—6 frog units, the equivalent in potency of approximately 0.1 g Foxglove leaf

Transparent, reddish brown liquid of bitter taste and characteristic odour, acid reaction

Administered orally, 10—15 drops 2—3 times a day

To be stored in a place protected from light observing safety precautions (List B)

d) Ciliated Foxglove preparations

DIGICILEN (*Digicilenum*)

Galenic preparation containing aqueous solution of total glycosides from above-ground parts of the Ciliated Foxglove (*Digitalis ciliata*), habitat—the Caucasus Preserved with 15% 96° ethanol

Transparent, almost colourless liquid of bitter taste 1 ml contains 6 frog units the equivalent in potency of 0.1 g Foxglove leaf

In its pharmacological properties indications and contraindications digicilen is similar to other Foxglove preparations

Mainly used in cases requiring immediate intervention, and when oral administration is impossible (because of vomiting, etc)

Administered subcutaneously and intramuscularly, 0.5—1 ml once or twice a day (beginning with 0.5 ml) The course of treatment consists of 6—12 injections

Available in ampoules of 1 ml

To be stored in a place protected from light, observing safety precautions (List B)

DIGICIL (*Digicilum*)

Galenic preparation containing the total glycosides of the Ciliated Foxglove Pale brown powder Available in tablets containing 5.5—6 frog units, the equivalent in potency of 0.1 g Foxglove leaf Adults are prescribed $\frac{1}{2}$ —1 tablet 2—3 times a day, length of treatment and precautionary measures are the same as for other Foxglove preparations

B. Adonis preparations

SPRING ADONIS or FALSE HELLEBORE *Adonis vernalis* L. perennial herb of Buttercup family (Ranunculaceae) found growing in the central zone and in the south of the European part of the USSR, in Central Asia and Siberia

For medicinal purposes the above ground parts (herb) of *Adonis* are used the stems with the leaves and partly with flowers or fruits (*Herba Adonidis vernalis*) 1 g of herb should contain not less than 50 frog units

The active principles of *Adonis* are glycosides, the most important being cymarin (see p 157) and adonitoxin, which consists of the aglycone, adonitoxigenin, and the sugar, rhamnose Cymarin is also the main active principle of Canadian hemp (*Apocynum cannabinum* L.)

In the character of their action the *Adonis* glycosides are similar to the Foxglove glycosides but they are considerably less stable in the body and have a shorter effect when therapeutic doses of *Adonis* are given there is practically no danger of cumulation Taken orally *Adonis* preparations are absorbed in amounts sufficient for obtaining a therapeutic effect

Adonis preparations are mostly used in chronic cardiac insufficiency they are also used as agents having a sedative effect on the central nervous system

Adonis Herb infusion is an ingredient of Bekhterev's a mixture which also contains sodium bromide and codeine (or codeine phosphate)¹ Adonisid, which is obtained from *Adonis* is an ingredient of the compound drug, cardiovalen

The potency of *Adonis* preparations like that of Foxglove preparations, must be checked periodically by biological assay

An infusion of *Adonis* Herb (*Infusum herbae Adonidis vernalis*) is prepared ex tempore for oral administration at a rate of 4, 6 or 10 g of herb per 200 ml Adults are prescribed 1 tablespoonful 3—5 times a day, children are given 1 teaspoonful or 1 dessertspoonful

Maximal doses for adults (calculated as dry herb) single — 1 g, daily — 5 g

Maximal doses for children 2 years old, single — 0.1 g daily — 0.4 g, 3—4 years, single — 0.15 g daily — 0.6 g, 5—6 years, single — 0.2 g daily — 0.8 g 7—9 years single — 0.3 g daily — 1.2 g, 10—14 years, single — 0.3—0.5 g daily — 1.2—2 g Children up to 2 years old are not prescribed *Adonis* infusion

Dry *Adonis* extract (*Extractum Adonidis vernalis siccum*) 1 g contains 50 frog units

"*Adonis* brom" tablets Sugar coated tablets containing 0.25 g dry *Adonis* extract and 0.25 g potassium bromide

Prescribed in a dosage of 1 tablet 3 times a day as a sedative and in chronic cardiac insufficiency

ADONISID (*Adonisidum*)

Water extract of Spring *Adonis* herb freed of inactive substances to the maximum, contains *Adonis* glycosides Transparent, slightly yellowish liquid with characteristic odour and bitter taste 1 ml contains 23—27 frog units² Adonisid is more highly purified from inactive substances than the preparation formerly put out under the name "Adonilen"

Used in cardiac insufficiency and neuroses Prescribed orally, intravenously and subcutaneously (subcutaneous injections are painful)

Orally, the preparation is administered 2—3 times a day adults — in doses of 15—20 drops, children — 1 drop for each year of their age Subcutaneously

¹ See also Bekhterev tablets p 32

² Adonisid has a greater frog unit content than Foxglove preparations because of the relatively low stability of the *Adonis* glycosides in the body

and intravenously, adults are given 0.5—1 ml once a day, children — 0.1—0.5 ml. When used over a lengthy period of time it is recommended that a 3—4 day break in treatment should be made every 5—6 days. When administered intravenously, adonisid is diluted with 10—20 ml 20% (40%) glucose solution. Injections must be made slowly (1 ml in 2—3 min).

Maximal doses for adults: single (orally and intravenously) — 1 ml, daily, orally, — 3 ml, daily, intravenously — 2 ml.

Maximal doses for children: orally, up to 6 months old, single — 1 drop, daily — 2 drops, from 6 months to 1 year, single — 2 drops, daily — 4 drops, 2 years — single — 3 drops, daily — 6 drops, 3—4 years, single — 5 drops, daily — 10 drops, 5—6 years — single — 6 drops, daily — 12 drops, 7—9 years, single — 8 drops, daily — 15 drops, 10—14 years, single — 10—15 drops, daily — 20—30 drops.

Contraindicated in pronounced organic changes in the heart and vessels. If the patient has been taking Foxglove preparations, a break of 4—6 days should be made before administering adonisid intravenously.

Available in vials of 15 ml for oral administration and in ampoules of 1 ml. To be stored in a cool place protected from light, observing safety precautions (List B).

Rp Adonisid 10
D t d N 6 in amp
S For intravenous administration
beginning with 0.5 ml
(in 10 ml 20% glucose solution)
once a day, gradually
increasing the dose to 1 ml
once a day

Rp Adonisid 150
DS 15 drops 2—3 times a day (for
an adult)
3 drops 2—3 times a day (for
3 year old child)

C Strophanthus preparations

The seeds of two species of strophanthus — *Strophanthus gratus* and *Strophanthus Kombé* Oliver — perennial tropical lianas of the Dogbane family (Apocynaceae), contain an extremely potent cardiac glycoside, strophanthin¹. According to the specifications of the USSR State Pharmacopoeia 1 g *Strophanthus* seed (*Semina Strophanthi*) shall contain not less than 2000 frog units.

In medical practice, strophanthin (synonyms *Kombetin*, *Oubain*, *Strophanthon*, *Purostrophanthin*) and tincture of *Strophanthus* seed are used.

STROPHANTHIN (*Strophanthinum*)

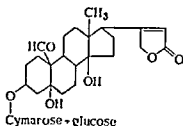
Two forms of strophanthin are recognized depending on the species from the seeds of which the glycoside is obtained, strophanthin K from *Strophanthus Kombé* and strophanthin G from *S. Gratus*; the latter is more potent. At present it is strophanthin K that is mostly used in the USSR for medicinal purposes. *Strophanthin G* is used as a standard in the biological assay of *Strophanthus* seed and preparations.

Strophanthin K — white crystalline powder, freely soluble in water (unlike Foxglove glycosides).

Synonym *Myokombin*.

¹ It has recently been established that strophanthin K is contained in 2 species of *Apocynum* found growing in the USSR — *Apocynum androsaemifolium* L. and *A. cannabinum* L. — as well as in the Golden Adonis (*Adonis chrysocyananthus* Hook. f. et Thoms.) (N. K. Ababukurov and R. S. Yamatova).

Made up of the aglycone, strophanthidin, and sugar (1 cymarose residue and 1 glucose residue)



Strophanthin possesses the basic properties of the cardiac glycosides, it is highly potent biologically (1 g strophanthin K contains about 40 000 frog units or about 6 500 cat units) and has a rapid and strong effect when administered intravenously. The systolic action is particularly marked in strophanthin. It has little effect on the frequency of the pulse and does not perceptibly block His bundle.

Strophanthin is one of the less stable glycosides and has little effect when taken orally. Practically speaking it has no cumulative effect, but if a patient has been receiving Foxglove preparations a break of at least 4 days must be made before administering strophanthin intravenously, since the effect of the strophanthin may be added to the effect of Foxglove glycosides that have accumulated in the body — this may cause toxic manifestations.

Strophanthin is used in acute cardiac insufficiency, chronic cardiac insufficiency (II B and III degree), paroxysmal tachycardia and the like.

Administered intravenously in the form of a 0.05% solution in doses of 0.00025—0.0005 g (0.5—1 ml 0.05% solution). The strophanthin solution is diluted with 10—20 ml 20% (40%) glucose. Injections must be made slowly (over a period of 5—6 min) — rapid administration may cause shock. Injections are given once (rarely twice) a day.

Maximal doses of 0.05% strophanthin solution intravenously for adults: single — 1 ml daily — 2 ml.

Maximal doses of 0.05% strophanthin solution for children (single and daily): 3—4 years — 0.1 ml, 5—6 years — 0.2 ml, 7—9 years — 0.25 ml, 10—14 years — 0.5 ml. Children up to 3 years old are not prescribed strophanthin.

Strophanthin's high potency and rapid effect make it necessary that there should be care and precision in the dosage and indications.

Contraindicated in pronounced organic changes in heart and vessels, acute myocarditis, endocarditis and advanced cases of atherosclerosis.

Overdosage of strophanthin may cause extrasystole, bigemina and dissociation of rhythm. In such cases the dose must be reduced and the intervals between injections increased. If there should be abrupt retarding of the pulse, injections are discontinued.

Available in ampoules containing 1 ml 0.05% solution.

To be kept locked (List A) in sealed ampoules in a place protected from light.

¹ When administering solutions of strophanthin and other heart glycosides glucose solution may be replaced by isotonic saline.

Rp Sol Strophanthini 0.05%, 10
D 1 d N 6 in amp
S 0.25—0.5 ml intravenously
(dilute with 10—20 ml glucose
solution, inject slowly!)

STROPHANTHUS TINCTURE (Tinctura Strophanthi)

Alcoholic tincture (10% tincture made with 70° alcohol) Transparent, brownish yellow liquid with faint characteristic odour and extremely bitter taste 1 ml contains 200 frog units or 26 cat units

Administered orally, adults — 3—6 drops, 2—4 times a day, children — 1—5 drops depending on the age At times 1—2 drops of Strophanthus tincture is administered intravenously with 5—10 ml 20% glucose solution To be injected slowly — over a period of at least 3—5 min (by the watch) More rapid intravenous administration may cause shock (Not to be confused with strophanthine solution when writing prescriptions or dispensing It must be remembered that 1 ml Strophanthus tincture contains 53 drops!)

Maximal doses for oral administration adults single — 0.2 ml (10 drops), daily — 0.4 ml (20 drops)

To be kept locked (List A) in well closed bottles

D. Lily-of-the-Valley preparations

The leaves and flowers (herb) of the common Lily of the Valley (*Folia et flores Convallariae majalis*, *Herba Convallariae majalis*) and of other species of Lily of the Valley, Lily family (Liliaceae), contain heart glycosides closely related in chemical structure to the Foxglove glycosides 1 g dried Lily of the Valley herb should contain 120 frog units

The principal Lily of the Valley glycosides are convallatoxin and convallaside The Lily of the Valley glycosides are distinguished by their low stability they have no cumulative effect When administered orally they act weakly They are mainly used in cardiac neuroses, often in combination with Valerian and Hawthorn preparations However, when administered intravenously Lily of the Valley preparations have a rapid and very strong influence on cardiac activity

In medical practice, Lily of the Valley tincture and extract are used as well as the crystalline glycoside, convallatoxin and the galenic preparations, convassid and corglycon which contain the total glycosides

LILY-OF-THE-VALLEY TINCTURE, Lily of the Valley drops (Tinctura Convallariae)

Prepared with 40° alcohol Transparent, greenish brown liquid with faint characteristic odour and bitter taste 1 ml contains 12 frog units

Administered orally adults — 15—20 drops 2—3 times a day, children — 1—12 drops

Maximal doses for children up to 6 months old, single — 1 drop daily — 3 drops, from 6 months to 1 year, single — 2 drops, daily — 6 drops 2 years single — 2 drops daily — 6 drops 3—4 years single — 4 drops daily — 12 drops, 5—6 years, single — 6 drops daily — 18 drops 7—9 years single — 7—10 drops daily — 20—30 drops 10—14 years single — 10—15 drops daily — 30—45 drops

DRY LILY-OF-THE-VALLEY EXTRACT (Extractum Convallariae siccum)

Amorphous hygroscopic powder, freely soluble in water

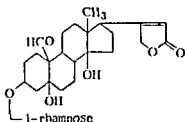
Available in powder form and in tablets containing 0.1 g concentrate, representing 12 frog units

Prescribed orally, 1 tablet 2—3 times a day

CONVALLATOXIN (Convallatoxinum)

Crystalline glycoside contained in the common Lily of the Valley White crystalline powder, sparingly soluble in water freely soluble in alcohol Melting point 212—213°

Closely related to strophanthin K in chemical structure Has the same aglycone as strophanthin — strophanthidin — but the sugar component is rhamnose



Possesses high biological potency 1 g contains about 75 000 frog units or about 10,500 cat units

When administered parenterally, especially intravenously, has a rapid and strong influence on cardiac activity Has only a slight cumulative effect.

When administered subcutaneously, the action is slower and weaker

When taken by mouth the potency is greatly reduced

When administered intravenously the effect sets in within 5—10 min, reaching a maximum in 1—2 hours and continuing up to 20—22 hours

In character of action convallatoxin is similar to strophanthin, and the indications for its use are the same

The preparation is administered intravenously, prescribed in smaller doses than strophanthin The single dose for adults is 0 00015—0 0003 g (0 15—0,3 mg) which corresponds to 0 5—1 ml 0 03% solution

Maximal dose of 0 03% solution intravenously, for adults single — 1 ml daily — 15 ml

Repeated injections (not exceeding the indicated daily dose) can be made at intervals of at least 8—10 hours The necessary dose of convallatoxin is injected in 10—20 ml 20% or 40% glucose solution, the injection is made slowly, over a period of 5—6 minutes inasmuch as rapid administration may cause shock

If the patient has previously been receiving Foxglove preparations, it is necessary to wait at least 4 days before administering convallatoxin

Care and precision in dosage and indications are necessary, the same as when strophanthin is used Contraindications are also the same as for strophanthin

Available in ampoules containing 1 ml of 0 03% aqueous solution (0 0003 g or 0 3 mg convallatoxin) The potency of 1 ml is 19—25 frog units or 2 8—3 5 cat units

To be kept locked (List A) in sealed ampoules in a place protected from light

CONVASID (Convasidum)

Galenic preparation obtained from the flowers of Lily of the Valley

Transparent yellowish liquid with characteristic odour and bitter taste pH=4 9—6 3

Available for parenteral and oral administration 1 ml contains 18—22 frog units When administered intravenously has a rapid and strong effect, similar to that of strophanthin but less pronounced

Administered intravenously or orally Subcutaneous injections are painful

Prescribed intravenously beginning with a dose of 0 2 ml daily, once a day or every other day depending on the patient's condition If there is good tolerance

rance the dose is gradually increased to 0.5 ml. Injections are made slowly over a period of 3–4 minutes (in 10–20 ml 20% or 40% glucose solution).

Orally, adults are prescribed 15–20 drops, 2–3 times a day, children — 1 drop for each year of their age.

Maximal single dose, intravenously, for adults 0.5 ml. Maximal daily dose 1 ml.

Contraindications are the same as for strophanthin.

If Foxglove preparations have been used previously, a break of 4–5 days must be made before administering convasid.

With the correct dosage, side effects are usually not observed. If there should be unpleasant sensations in the region of the heart the dose is reduced and intervals between injections increased. If there should be an abrupt retarding of the pulse injections are discontinued.

Available in ampoules of 1 ml and in vials of 15 ml.

To be stored in a cool place protected from light observing safety precautions (List B).

Rp Convasid 10
D t d N 6 in amp
S 0.2–0.5 ml intravenously in
10 ml 20% glucose solution
(inject slowly!)

Rp Convasid 150
DS 15 drops 3 times a day

CORGLYCON (Corglyconum)

Preparation containing the total glycosides of the leaves of Lily of the Valley freed of inactive substances. Slightly yellowish amorphous powder odourless bitter taste freely soluble in alcohol and acetone sparingly soluble in water and chloroform insoluble in ether.

An aqueous solution containing 0.6 mg corglycon per ml is used. Preserved with chlorobutanol. Transparent colourless liquid of bitter taste with odour of chlorobutanol. Potency 1 ml represents 8–10 frog units.

Corglycon is analogous in action to other purified Lily of the Valley preparations similar to strophanthin when administered intravenously.

The effect is rapid and powerful but of shorter duration than that of strophanthin (after a single injection the effect lasts 6–10 hours).

Administered intravenously adults — 0.5–1 ml per injection children from 2 to 5 years old — 0.2–0.5 ml from 6 to 12 years — 0.5–0.75 ml. Not infrequently injections must be given twice a day. Injections are made slowly (over a period of 5–6 min) in 10–20 ml 20% or 40% glucose solution.

Maximal doses intravenously for adults single — 1 ml daily — 2 ml.

Contraindications are the same as for strophanthin.

To be stored in a cool place protected from light observing safety precautions (List B).

Rp Sol Corglycon 0.06% 10
D t d N 10 in amp
S 0.5–1 ml intravenously in 20 ml
40% glucose solution (inject slowly!)

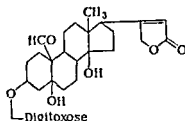
E Erysimum preparations

Preparations from 2 species of Erysimum are being used today in medical practice. Hoary Erysimum (*Erysimum canescens* Roth.) and Treacle Erysimum (*E. cheiranthoides* L.) family Cruciferae found growing in various parts of the USSR.

The active principles of Erysimum are glycosides similar in action to the glycosides of the Foxglove group.

ERYSIMIN (Erysimum)

Crystalline glycoside from the Hoary Erysimum. White crystalline powder, soluble in water (1:60 at room temperature), freely soluble in alcohol and ether. Melting point 168—172°. Consists of the aglycone strophanthidin and the sugar digitoxose.



Erysimin possesses high biological potency (1 g contains 62,500 frog units or about 10,500 cat units) has rapid and powerful effect when administered intravenously. In some cases the clinical effect is not inferior to that of strophanthin at times it is tolerated better.

Indications for use the same as for strophanthin especially effective in patients with mitral disease. The diuretic effect observed when erysimum is used is associated with the improvement in cardiac activity.

Administered intravenously in doses of 0.5—1 ml of 1:3000 solution (0.33 mg crystalline glycoside per ml) for adults. Injected slowly in 20 ml 40% glucose solution or isotonic saline. The daily dose is usually 1 ml.

Maximal doses of 0.033% solution intravenously for adults: single—1 ml daily—2 ml.

Contraindications possible complications and precautionary measures are the same as when using strophanthin.

Available in ampoules containing 1 ml 0.033% solution (1:3000). Potency 1 ml represents 18—22 frog units.

To be kept locked (List A) in sealed ampoules in a place protected from light.

Rp Sol Erysimini 0.033% 10

D t d N 6 in amp

S 0.5—1 ml intravenously in 20 ml

40% glucose solution (inject slowly)

CORESID (Coresidum)

Preparation containing the total glycosides of Erysimum cheiranthoides.

Amorphous yellow powder odourless bitter taste sparingly soluble in water freely soluble in alcohol and chloroform insoluble in ether.

1 g of the preparation corresponds in potency to 55,000 frog units or 5,800 cat units. Similar in pharmacological properties to other Erysimum preparations.

Administered intravenously in the form of a 0.05% aqueous solution chiefly in acute and chronic insufficiency of the circulation (II and III degree) 0.5—1 ml in 10—20 ml 40% glucose solution injected once or twice a day. Course of treatment 10—30 injections.

Contraindications possible complications and precautionary measures are the same as when using strophanthin and erysimum.

Available in ampoules containing 1 ml 0.05% solution Potency 1 ml represents 26—29 frog units

To be kept locked (List A) in sealed ampoules in a place protected from light

Rp Sol Coresidi 0.05% 10
D t d N 6 in amp
S 0.5 ml intravenously in 10 ml
40% glucose solution

CARDIOVALEN (Cardiovalenum)

Compound preparation of the following composition juice of fresh Hoary Erysimum having a potency of 150 frog units per ml (or Erisid extract of the same potency) — 17 parts, Adonisid (extract having potency of 85 frog units per ml) — 30 parts fluid extract of Red Haws — 2 parts tincture of freshly gathered Valerian rhizomes and roots (or ordinary Valerian tincture) — 46.9 parts, camphor — 0.4 part, sodium bromide — 2 parts, 96° alcohol — 1.6 parts, chlorobutanol up to 0.25%

Light brown liquid, salty bitter taste, odour of camphor and Valerian

The biological potency is determined from the number of units represented by the Erysimum and Adonisid content 1 ml contains 45—55 frog units

Used in rheumatic heart disease, cardiosclerosis with symptoms of cardiac insufficiency, and impaired circulation of I II and III degree, as well as in stenocardia (without organic changes in the cardiac vessels) and autonomic neuroses

Administered orally, 15—20 drops once or twice a day Course of treatment 20—30 days

Available in vials of amber glass containing 15 ml

To be stored in a cool place protected from light observing safety precautions (List B)

Rp Cardiovaleni 15.0
DS 15—20 drops once or twice
a day

F. Canadian Hemp preparations

Canadian Hemp (*Apocynum cannabinum* L.), Dogbane family (Apocynaceae)

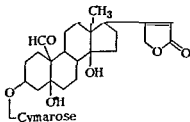
Perennial herb, habitat — North America cultivated in the USSR

Preparations obtained from the roots of Canadian Hemp are used in medical practice They contain glycosides, the most important being cymarín

CYMARIN (Cymarinum)

White crystalline substance, sparingly soluble in water freely soluble in alcohol and chloroform insoluble in ether Melting point 142—144°

Consists of the aglycone, strophanthidin, and the sugar cymarose It follows that it differs from strophanthin only in the sugar residue



Cymarín is biologically highly potent—1 g contains approximately 45 000 frog units or 6 600 cat units. Similar to strophanthin in character of action has rapid effect when administered intravenously, has pronounced diuretic action in cases of edema. Cumulative properties less marked than in Foxglove preparations but may be manifested if used for lengthy periods.

Indications for the use of cymarín are the same as for strophanthin. Administered intravenously, 0.5—1 ml 0.05% solution (1:2 000) in 15—20 ml 20—40% glucose solution or isotonic saline, once or twice a day (to be injected slowly!).

Maximal doses of 0.05% solution intravenously, for adults single—1 ml, daily—1.5 ml.

Course of treatment 10—20 injections. In order to avoid manifestations of cumulation a break of 1—2 days must be made after every 3—5 injections.

Contraindications and precautionary measures are the same as when using strophanthin. In cases of abrupt retarding of the pulse, attacks of stenocardia, or nausea injections are discontinued.

Available in ampoules containing 1 ml 0.05% solution. Potency 1 ml represents 20—22 frog units.

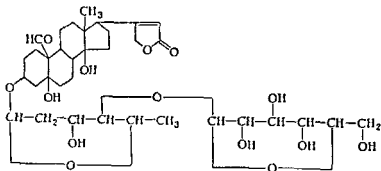
To be kept locked (List A) in sealed ampoules in a place protected from light.

Rp Sol Cymarini 0.05% 10
D t d N 6 in amp
S 0.5 ml intravenously in 10 ml
40% glucose solution (inject slowly!)

G Jute preparations

OLITORISIDE (Olitorisidum)

Glycoside isolated from the seeds of the Polsherb Jute (*Corchorus olitorius*), Linden family (Tiliaceae) cultivated in the southern regions of the USSR as a source of fibre for yarn.



White crystalline substance, bitter taste, sparingly soluble in water, freely soluble in alcohol. Melting point of anhydrous glycoside 202—207°.

Consists of the aglycone, strophanthidin, joined to two molecules of sugar, bovinose and glucose. Possesses high biological potency 1 g represents approximately 60 000 frog units.

In pharmacological properties, olitoriside is similar to strophanthin. Like the latter it has a strong systolic effect and does not possess cumulative properties.

Indications for use are the same as for strophanthin.

Olitoriside is administered intravenously in the form of a 0.04% solution, the dose for adults is 0.5—1 ml daily. Course of treatment 10—15 days.

Contraindications, possible complications and precautionary measures are the same as for strophanthin

Available in ampoules containing 1 ml 0.04% solution Potency 1 ml represents approximately 25 frog units

To be kept locked (List A) in sealed ampoules in a place protected from light

Rp Sol Olitorisidi 0.04% 10
D t d N 6 in amp
S 0.5 ml intravenously once a day

H. Silk-vine preparations

Silk vine (*Periploca graeca* L.), bush of Milkweed family (Asclepiadaceae) grows in southern part of the Ukraine, the Caucasus and Moldavia

Contains the glycoside periplocin which has a potent cardiac effect

PERIPLOCIN (Periplocinum)

Glycoside from the bark of the Silk vine White crystalline substance, bitter taste sparingly soluble in water (1:125), freely soluble in alcohol Melting point 205—206°

Consists of the aglycone, periplogenin which is closely related to strophanthin, and sugar residues — cymarose and glucose

Periplocin is a potent cardiac agent, approximates strophanthin in pharmacological properties but is inferior in the speed and strength of effect

Periplocin is mainly used for patients with insufficiency of circulation of IIA and IIB degree In cases of serious insufficiency of circulation it is recommended that strophanthin should be used the first few days going over to periplocin when the condition has improved

Periplocin is administered intravenously less frequently subcutaneously Subcutaneous injections are painful and may be accompanied by reddening of the skin at the site of injection Intravenous administration is to be preferred (in 5—20 ml 40% glucose solution or isotonic saline)

The preparation is prescribed in doses of 0.000125—0.00025 g (0.5—1 ml 0.025% solution) once or twice a day The course of treatment consists of 10—30 injections, depending on the patient's condition

Maximal doses of 0.025% solution, intravenously for adults single — 1 ml daily — 2 ml

There are usually no side effects or manifestations of cumulation when periplocin is used Nevertheless if Foxglove has been given previously, administration of periplocin, as of similar preparations, should be commenced only after a five day interval

Available in ampoules containing 1 ml 0.025% solution

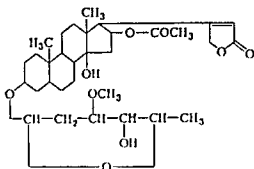
To be kept locked (List A) in sealed ampoules in a place protected from light.

Rp Sol Periplocini 0.025% 10
D t d N 3 in amp
S 0.5—1 ml intravenously in
20 ml 40% glucose solution
(inject slowly!)

I. Oleander preparations

Oleander (*Nerium oleander* L.), evergreen bush of Dogbane family (Apocynaceae), cultivated along the Caucasian and Crimean coast of the Black Sea as well as in Azerbaijan as a decorative plant

The leaves of the Oleander contain glycosides oleandrin (folinerin), adonin and nerolin Oleandrin which has a potent cardiac effect consists of the aglycone oleandrogenin or 16 acetylglitoxigenin and the sugar, oleandrose



Oleandrin is available for medical use under the name "Neriolin"
NERIOLIN (Neriolinum)

White crystalline substance sparingly soluble in water freely soluble in alcohol and chloroform Melting point $240-241^{\circ}$

Potency 1 g crystalline neriolin represents 37,500 frog units or approximately 3,800 cat units The preparation is highly active and is absorbed well when taken orally Similar to Foxglove in the character of its effect but acts more quickly (in 4-8 hours) and has less pronounced cumulative properties

Neriolin is administered orally in the form of tablets or solutions in acute and chronic insufficiency of circulation of II and III degree, especially in mitral disease with fluttering arrhythmia

The dosage is 1 tablet (0.0001 g = 0.1 mg) 3 times a day or 20-25 drops of 0.02% alcoholic solution (1:5000) twice a day In order to avoid a cumulative effect it is recommended that a 4-5 day break in treatment should be made every 10 days The length of the course of treatment depends on the course of the disease and the patient's condition, the course of treatment is usually 10-40 days

Maximal doses for adults single — 0.0002 g (0.2 mg), daily — 0.0004 g (0.4 mg)

Contraindications are the same as for Foxglove

Available in 1:5000 solution in 70% alcohol in vials of 10 ml (1 ml contains 7-8 frog units) and in tablets of 0.1 mg (35-4 frog units).

To be kept locked (List A) in well closed bottles in a place protected from light The potency is checked every year

Rp Neriolini 0.0001
D t d N 10 in tabul
S 1 tablet 3 times a day

Rp Sol Neriolini spirituosae
0.02% 100
DS 20 drops twice a day

J. Hellebore preparations

Black Hellebore (*Helleborus purpurascens* W et K *H. niger* L.) and Caucasian Hellebore (*H. caucasicus*), perennial herbs of the Buttercup family (*Ranunculaceae*)

The former species grows in the southern and southwestern parts of the USSR, the latter grows in the Caucasus Both contain cardiac glycosides The

glycoside from Black Hellebore is known as corelborin P that from Caucasian Hellebore — corelborin K

CORELBORIN (Corelborinum)

Corelborin P crystalline substance sparingly soluble in water (0.05%) acetone and chloroform more soluble in ethanol Melting point 261—264°

Corelborin K crystalline substance also sparingly soluble in water but unlike corelborin P freely soluble in acetone Melting point 232—234°

In chemical structure both glycosides belong to the Squill subgroup since they have a six membered ring in the aglycone Corelborin K contains rhamnose as the sugar residue corelborin P contains rhamnose and glucose

The two glycosides are similar in action Corelborin K is more potent — 1 g contains 88 000 frog units while 1 g corelborin P contains 66 000 frog units

In rapidity of the effect the two glycosides approximate strophanthin in duration of effect and cumulative properties they are similar to Foxglove

Used for patients with decompensated cardiac activity when a rapid and lengthy effect is required

The two glycosides are effective when administered orally or intravenously but the effect is more pronounced when given intravenously

The method of administration and the dosage should be individualized depending on the character of the disease tolerance for the preparation etc The average single therapeutic dose intravenously for both glycosides is 0.0002—0.00025 g (0.2—0.25 mg) To be injected slowly in 10—20 ml 20% (40%) glucose solution Injections are given once a day Orally corelborin K is prescribed in single doses of 0.0002 g and up to 0.0006 g daily corelborin P — single doses of 0.0002 g and up to 0.0008 g daily

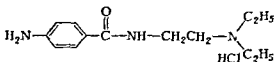
Contraindications are the same as for Foxglove preparations

Corelborin P and corelborin K are available in tablets of 0.0002 g (0.2 mg) and in ampoules containing 1 ml 0.0025% solution (0.25 mg)

To be kept locked (List A) in a place protected from light

II AGENTS LOWERING THE EXCITABILITY OF THE MYOCARDIUM

PROCAINAMIDE (Procainamidum)



Synonyms Novocainamid Novocamid Procainamid₁ hydrochloridum, Pro nestyl

Yellowish pink powder freely soluble in water Melting point 165—168° Solutions turn yellow on standing but pharmacological properties do not change substantially

Closely related in chemical structure to procaine (see p 196) instead of the ester group of procaine (—CO O—) contains an amide group (—CO NH—) In pharmacological properties also similar to procaine and has a local anesthetic effect Nevertheless the most important pharmacological property of procainamide is its ability greatly to lower the excitability and conductivity of the myocardium in this respect it is considerably more potent than procaine Procainamide is more stable than procaine since it is considerably more slowly destroyed by the enzymes of the blood plasma It is likewise less toxic than procaine

Procainamide is used in various disorders of cardiac rhythm paroxysmal fluttering arrhythmia paroxysmal tachycardia extrasystole and other cases of

Impaired rhythm It is employed in operations on the heart, great vessels and lungs to prevent or treat disorders of cardiac rhythm arising during surgical intervention

Administered orally intramuscularly or intravenously When used orally a preliminary trial dose of 0.5 g is given. If there are no side effects treatment is continued prescribing oral doses of 0.5–1 g and bringing the daily dose up to 3–4 g. The length of treatment depends on the effectiveness and tolerance usually the drug is prescribed for 4–5 days. Intramuscularly, injections of 5–10 ml 10% solution (0.5–1 g of the drug) are given bringing the daily dose up to 20–40 ml (2–4 g of the drug). Administration is continued until a sinus rhythm is restored. If symptoms of a toxic effect should appear injections are discontinued. If paroxysmal tachycardia has not disappeared in 72 hrs procainamide is withdrawn. After the restoration of a sinus rhythm the drug is prescribed in a dose of 0.5 g (5 ml 10% solution) 3–4 times a day for the next 2 days.

Procainamide is administered intravenously in cases requiring urgent intervention in serious disorders of cardiac rhythm arising during operations on the heart and lungs and in collapse developing as a consequence of paroxysmal arrhythmia etc. 2.5 or 10 ml 10% solution is injected the injection is given slowly preferably by the drip method (in glucose solution or isotonic saline). During the intravenous administration the patient's condition must be carefully observed and the arterial pressure measured. If the drug is rapidly injected into the vein the blood pressure may fall abruptly with symptoms of collapse. If necessary mesaton is injected repeatedly in such cases (0.3–0.1 ml 1% solution). Intravenous infusion of procainamide is repeated in 1–2 hours if the electrocardiogram recorded at that time reveals no symptoms of impaired conductivity of the myocardium.

During anesthesia in surgical operations procainamide is administered intravenously if necessary in a dose of 0.1–0.5 g at a rate of 0.1 g (1 ml 10% solution) per min.

When using procainamide it must be remembered that the drug may cause side effects. Besides a collapsoid reaction which is a possible consequence of intravenous administration the following symptoms may be observed whatever the method of administration: general weakness, headache, nausea, emesis, excitement and insomnia. There may be a bitter taste in the mouth.

In cases of overdosage and heightened individual sensitivity cardiac activity may be depressed and ventricular fibrillation may develop.

Treatment with procainamide should not be undertaken in cardiac block, marked sclerotic changes in the heart and vessels or pronounced cardiac insufficiency. The drug is categorically contraindicated if there is heightened individual sensitivity.

Available in tablets of 0.25 g in hermetically closed vials containing 10 ml 10% solution and in ampoules containing 5 ml 10% solution.

To be stored in a place protected from light observing safety precautions (List B).

HAWS (Fructus Crataegi)

Dried fruits of the English Hawthorn (*Crataegus oxyacantha* L.) or the Red Hawthorn (*C. sanguinea* Pall.) Rose family (Rosaceae).

The fruits contain choline, acetylcholine, tannin, fructose, phytosterin-like substances. The flowers of the Hawthorn contain quercetin, quercitrin, volatile oil and other substances.

Hawthorn preparations somewhat strengthen the contractions of the myocardium while at the same time reducing its excitability.

It has lately been established that Hawthorn contains terpenic acids — oleanolic, ursolic and crataegic — which intensify circulation in the coronary and cerebral vessels and heighten the sensitivity of the heart to cardiac glycosides. The pharmacological properties of Hawthorn preparations have not been studied sufficiently.

Hawthorn preparations are being used today in functional disorders of cardiac activity, angioneuroses, fluttering arrhythmia and paroxysmal tachycardia (in addition to quinidine, quinine or procainamide)

Administered in the form of a fluid extract of the fruits or a tincture of the flowers

Rp Extr Crataegi fluidi 250
DS 20—30 drops 3—4 times a day
(before meals)

Rp T rae Crataegi 200
DS 20—30 drops 3—4 times a day
(before meals)

III. AGENTS WHICH RELAX THE SMOOTH MUSCLES OF THE BLOOD VESSELS, OF THE BRONCHI AND THE ORGANS OF THE ABDOMINAL CAVITY (SPASMOLYTIC AGENTS)

A. Nitrites and nitrates

Organic and inorganic nitrites (compounds containing the NO_2 group) and organic nitrates (which contain the NO_2 group) have long been used in medical practice to abort attacks of angina pectoris and to lower the arterial pressure in hypertensive disease. The principal representatives of the nitrite group are amyl nitrite and sodium nitrite; the principal organic nitrate is nitroglycerol. Lately other organic nitrites have been proposed (octyl nitrite, etc.), as well as other nitrates (nitranol, nitropeptone, etc.). Inorganic nitrates are not used because of their low effectiveness.

The use of nitrites and nitrates is based on their ability to cause dilation of the blood vessels; this effect is due both to their direct influence on the smooth muscles of the walls of vessels, and partially to the reflex inhibition of the vasomotor centres (especially true of amyl nitrite). Recent experimental findings show that the action of nitroglycerol is also associated with the influence on the interoreceptors of the coronary vessels (V. V. Zakusov).

What is most significant is the influence of the substances of this group on the walls of the arterioles but they also cause relaxation of the smooth muscles of the veins, the gastrointestinal tract, the bile ducts, the uterus and other organs. The adverse aspect of the action of nitrites is dilation of the veins and the possible development of collaptoid reactions.

Nitrites cause a substantial lowering of the arterial pressure particularly in hypertension. At present however, they are practically not used for the treatment of hypertensive disease since the hypotensive effect may be accompanied by side effects (collapse, reduction of the blood supply of the kidneys, etc.), besides this the effect is not constant or prolonged, patients quickly become accustomed to nitrites and the hypotensive effect becomes progressively less pronounced on repeated administration.

The principal use of nitrites is in angina pectoris, they quickly induce dilation of the coronary vessels and abort the pain syndrome.

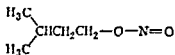
Nitrates are likewise extensively used in angina pectoris, nitroglycerol particularly finds wide application. Because of the differences in chemical structure of the various nitrates, and the peculiarities of their pharmacological action, particularly the rapidity of onset of the coronary dilating effect and its duration they are employed for different purposes. Nitroglycerol is quickly absorbed by the mucous membranes and has an almost immediate effect. Nitranol and other drugs are absorbed more slowly but their action is more prolon-

ged For that reason nitroglycerol is chiefly used to abort attacks of angina pectoris while nitranol is used to prevent attacks as well as in less acute manifestations of spasm of the coronary vessels

The mode of action of nitrites and nitrates has not been sufficiently investigated It has been suggested that nitrates are decomposed in the body with the formation of nitrite ions which have the main pharmacological effect Experimental and clinical findings however (the action of nitrates in considerably less doses than nitrites and the rapid effect of nitroglycerol), run counter to this conception

AMYL NITRITE (*Amylium nitrosum*)

Nitrous acid ester of Isoamyl alcohol



Synonyms Isomilnitrit Vaporole

Transparent light yellow mobile extremely volatile liquid characteristic fruity odour soluble in alcohol ether and chloroform almost insoluble in water

Inhaling the vapours of amyl nitrite causes rapid but transitory dilation of the blood vessels dilation of the coronary and cerebral vessels is especially marked The vasodilator effect is associated with depression of the vasomotor centre (partially due to reflex influence of the chemoreceptors of the carotid gland) and with the direct influence on the walls of the vessels Dilation of the vessels is accompanied by lowering of the arterial pressure and reflex acceleration of cardiac activity

Used to abort attacks of stenocardia and sometimes in embolism of the central artery of the retina

Also employed as an antidote in poisoning with hydrogen cyanide and its salts this is due to the ability of amyl nitrite (and other nitrites) to cause the formation of methemoglobin in the blood methemoglobin binds the CN ion, in this way protecting the respiratory enzymes of the tissues

Amyl nitrite is administered by inhalation after application to a handkerchief or to a piece of cotton or gauze Adults are given 2—3 drops children over 5 years old — 1—2 drops

Maximal doses for adults (for inhalation) single — 5 drops daily — 30 drops

In cases of poisoning with cyanides the designated doses are given repeatedly (up to a total dose of 0.5—1 ml)

Amylnitrite (as well as other nitrites and nitrates) causes an elevation of the intraocular pressure for that reason glaucoma is a contraindication to its use

Available in ampoules of amber glass containing 0.5 ml There is a slight explosion when ampoules are opened because of the pressure of the vapours formed during storage and heating Amyl nitrite vapours form an explosive mixture with air

To be stored in sealed ampoules in a cool place protected from light observing safety precautions (List B)

Rp Amyli nitrosi 0.5

℞ 1 & 1/2 in amp

S 2—3 drops on handkerchief
to be inhaled in attack of
stenocardia

SODIUM NITRITE (*Natrium nitrosum*) NaNO_2

White crystals with pale yellowish tint hygroscopic freely soluble in water (1/15) sparingly soluble in alcohol Aqueous solution has weak alkaline reac

tion Solutions are sterilized by holding at 100° for 30 min Solutions are stabilized by the addition of 2 ml 0.1 N sodium hydroxide per litre

Mainly used orally as a vasodilator in stenocardia The action is similar to that of amyl nitrite, the effect develops more slowly but is more lengthy

Single dose (0.5% solution) — 0.1—0.2 g

Maximal doses for adults (orally) single — 0.3 g, daily — 1 g

Sodium nitrite is also used in poisoning with cyanides, in such cases — 10—20 ml 1—2% solution is administered intravenously

To be stored in well closed bottles of amber glass in a place protected from light observing safety precautions (List B)

NITROGLYCEROL (Nitroglycerolum)

Glycerol trinitrate



Synonyms Glonoin, Glyceryl trinitrate Nitrangin, Nitracardiol, Nitroglycerin, Nitromint, Trimitrin, Trimitroglycerol Trinitrol

Colourless oily liquid sparingly soluble in water, freely soluble in alcohol, ether, chloroform Used in medical practice in the form of a 1% alcoholic solution and in tablets

Nitroglycerol solution (Solutio Nitroglyceroli spiritiosa 1% Nitroglycerolum solutum) — 1% alcoholic solution of nitroglycerol Transparent colourless liquid of neutral reaction Sp gr 0.814—0.830

Nitroglycerol is easily absorbed by the mucous membranes and the intact skin It is not decomposed in the stomach but is less effective when administered in this way than when absorbed through the mucous membrane of the mouth

Used in stenocardia, chiefly to abort acute attacks of spasms of the coronary vessels It is little suited for preventing attacks because of the transitory effect Between attacks, drugs of the organic nitrate group (nitranol, nitropeptone), which have a slower but more protracted action are used, or drugs like papaverine, aminophylline, tiphen, etc. The use of nitroglycerol is not expedient in patients with myocardial infarction in the acute stage of coronary thrombosis (M S Vovsi et al), nitroglycerol should not be prescribed when the arterial pressure is low

Nitroglycerol is occasionally employed in embolism of the central artery of the retina, as well as in functional cholecystopathy

Nitroglycerol is administered in 1% solution 1—2 drops are applied to the tongue, or 2—3 drops are applied to a small piece of sugar which is held in the mouth without swallowing until it has completely dissolved

Maximal doses for adults single — 4 drops daily — 16 drops

When nitroglycerol is used headache, a roaring in the ears and vertigo may be observed An abrupt fall in arterial pressure may sometimes develop, with symptoms of collapse

Solutions must be prevented from coming into contact with the skin as the drug can be absorbed causing a severe headache

Care must be taken when working with nitroglycerol (when pouring the solution from one container to another, when weighing etc) since there may be an explosion if a large amount is spilled and the alcohol evaporates

Available in bottles containing 5 and 10 ml of 1% solution

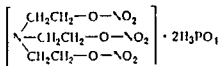
To be kept in well closed bottles in a cool place protected from light and at a distance from fire, observing safety precautions (List B)

Nitroglycerol tablets (Tabulettae nitroglyceroli) (List B)

Specially prepared tablets containing 0.0005 g (0.5 mg) nitroglycerol. The total weight of the tablet is 0.027 g (sugar, glucose and starch are used as fillers). Prescribed in doses of 1/2—1 tablet. The tablet is held under the tongue until completely dissolved.

AMINOTARTRATE PHOSPHATE.

Diphosphate of triethanolamine trinitrate



Synonyms Metamine Nitralettas Nitranol Nitretamine phosphate Ortin Praenitron

White fine crystalline powder sparingly soluble in water soluble in alcohol. Melting point 106—110°

Causes dilation of the coronary vessels acts more slowly than nitroglycerol but the effect is more protracted. The effect after a single administration may last up to 5 hours. In therapeutic doses does not cause a lowering of the arterial pressure. Is readily absorbed by the mucosa of the gastrointestinal tract.

Chiefly used to prevent attacks of stenocardia.

The drug is tolerated well and side effects are usually not observed. May also be used in spasms of the peripheral vessels (intermittent lameness and the like). Prescribed orally in tablets in a dosage of 0.002 g 3—4 times a day after meals. Tablets should be swallowed without chewing. Contraindicated in glaucoma.

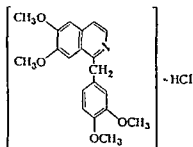
Available in tablets of 0.002 g (2 mg). Safety precautions to be observed during storage (List B).

B Isoquinoline derivatives

PAPAVERINE HYDROCHLORIDE (Papaverinum hydrochloricum Papa-verini hydrochloridum)

Hydrochloride of the alkaloid papaverine, which is contained in opium. Also produced synthetically.

6734 Tetramethoxybenzylisoquinoline hydrochloride



White crystalline powder of slightly bitter taste slowly dissolves in water on constant stirring (1:40) sparingly soluble in alcohol. Aqueous solutions are sterilized by holding at 100° for 30 min.

Papaverine has a slight depressing influence on the central nervous system but its principal property is the ability to cause lowering of the tone and relaxation of the smooth muscles

Papaverine is widely employed as a spasmolytic in spasms of the blood vessels (in hypertension stenocardia and migraine) spasms of the smooth muscles of the abdominal organs (pylorospasm cholecystitis spastic colitis and spasms of the urinary tract) and bronchial asthma. Often used in combination with sedatives and other spasmolytics (phenobarbital bromisovalum salsoline aminophylline theobromine sodium salicylate etc)

Administered orally in powders and solutions in a dosage of 0.02—0.05 g, 2—4 times a day and subcutaneously in 1—2% solution in doses of 1—2 ml

Maximal doses for adults single—0.15 g daily—0.5 g

Maximal doses for children from 6 months to 1 year old single—0.005 g, daily—0.01 g 2 years single—0.01 g, daily—0.02 g 3—4 years single—0.015 g daily—0.03 g 5—6 years single—0.02 g, daily—0.04 g 7—9 years single—0.03 g daily—0.06 g 10—14 years single—0.05 g, daily—0.1 g Infants up to 6 months old are not prescribed papaverine

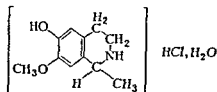
Available in powder form and in tablets of 0.015 and 0.02 g Compound tablets of the following composition are also available a) papaverine hydrochloride—0.02 g and phenobarbital—0.02 g, b) papaverine hydrochloride—0.02 g, phenobarbital—0.02 g and salsoline hydrochloride—0.03 g c) papaverine hydrochloride—0.02 g and theobromine—0.02 g, d) papaverine hydrochloride—0.02 g dibazol—0.02 g and theobromine—0.15 g e) papaverine hydrochloride—0.03 g, salsoline hydrochloride—0.03 g and theobromine—0.2 g Tablets are likewise available containing papaverine in combination with platyphylline aminophylline aminopyrine amobarbital sodium and other drugs

To be kept in bottles with ground glass stoppers in a place protected from light observing safety precautions (List B)

SALSOLINE HYDROCHLORIDE (Salsolinum hydrochloricum)

Salsoline is an alkaloid from *Salsola Richteri* Kar Goosefoot family (Che nopodiaceae) habitat—Central Asia

For medical purposes the hydrochloride of salsoline is used—1 methyl 6 hydroxy 7 methoxytetrahydroisoquinoline hydrochloride



White (or white with a very pale yellowish tint) crystalline powder odour less bitter taste soluble in water (1:14) sparingly soluble in alcohol Melting point (after drying at 100—105°)—197—203° Aqueous solutions are sterilized by holding at 100° for 30 min

Salsoline dilates the blood vessels and causes a moderate lowering of the arterial pressure. It has a general sedative effect and is only slightly toxic.

Used in hypertensive disease and in spasms of the cerebral vessels

Administered orally in doses of 0.03 g 3 times a day or subcutaneously—1 ml 1% aqueous solution once or twice a day To increase the effect it is recommended that salsoline should be combined with theobromine sodium salicylate phenobarbital papaverine or other sedative and hypotensive agents

Maximal doses for adults single—0.1 g daily—0.3 g

Contraindicated in decompensation of cardiac activity and serious impairment of the functions of the liver and kidneys

Available in powder form and in tablets of 0.03 g

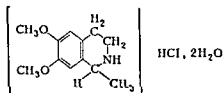
To be stored in well closed bottles of amber glass, observing safety precautions (List B)

- Rp Salsolini (s Salsolidini)
hydrochlorici 003
D t d N 12 in tabul
S 1 tablet 3 times a day
- Rp Salsolini (s Salsolidini) hydrochlorici
003
Papaverini hydrochlorici
Phenobarbitali aa 002
D t d N 12 in tabul
S 1 tablet 3 times a day
- Rp Salsolini (s Salsolidini) hydrochlorici
003
Phenobarbitali 005
D t d N 12 in tabul
S 1 tablet 3 times a day
- Rp Salsolini hydrochlorici 003
Aminopyrini 03
Theobromini 025
D t d N 10 in tabul
S 1 tablet 3 times a day
- Rp Salsolini hydrochlorici
Papaverini hydrochlorici aa 003
Theobromini 025
D t d N 10 in tabul
S 1 tablet 3 times a day
- Rp Salsolini hydrochlorici
Phenobarbitali aa 003
Theobromini 015
Aminopyrini 03
D t d N 10 in tabul
S 1 tablet 3 times a day
- Rp Sol Salsolini hydrochlorici 1% 100
Sterilisetur!
DS 1 ml subcutaneously once or twice a day

SALSOLIDINE HYDROCHLORIDE (Salsolidinum hydrochloricum)

Salsolidine is an alkaloid contained along with salsoline in Salsola Richteri

For medical purposes the hydrochloride of salsolidine is used — 1 methyl 6 hydroxy 7 methoxytetrahydroisoquinoline hydrochloride



White (or white with a very pale yellowish tint) crystalline powder, soluble in water (1:15) Melting point 215°

Similar to salsoline in pharmacological properties and therapeutic action Causes a lowering of the arterial pressure and improves the general condition of patients in the first stages of hypertensive disease

Administered orally in a dosage of 0.02—0.03 g 3 times a day for 10—15 days running, the length of the subsequent interval depending on the way the patient feels and the level of the arterial pressure. Contraindications are the same as for salsoline.

Maximal doses for adults: single — 0.1 g, daily — 0.3 g.

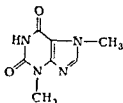
Available in powder form and in tablets of 0.03 g.

To be kept in well closed bottles in a dry place protected from light, observing safety precautions (List B).

C. Purine derivatives

THEOBROMINE (Theobrominum)

Alkaloid obtained from hull of cacao beans (*Semina Cacao*), also produced synthetically. 3,7-Dimethylxanthine.



White crystalline powder of bitter taste, very slightly soluble in cold water (1:700), sparingly soluble in hot water, freely soluble in dilute alkalis and acids.

Related in chemical structure and similar in pharmacological properties to other alkaloids of the purine series. Has a stimulating influence on cardiac activity, dilates the coronary vessels and the bronchial muscles and intensifies urysis. The diuretic effect of theobromine and related compounds is chiefly associated with diminished tubular reabsorption of water and sodium and chloride ions; tubular filtration does not change significantly. Theobromine stimulates the central nervous system to a lesser degree than caffeine.

Mainly used in spasms of the vessels of the heart and in edema of cardiac and renal origin.

Administered orally after meals in doses of 0.25—0.5 g once or twice a day (for adults).

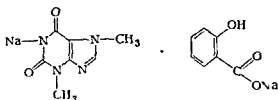
Maximal doses for adults: single — 0.5 g, daily — 2 g.

Theobromine is often used in the form of the sodium salt combined with sodium salicylate with which it forms a complex (see Theobromine sodium salicylate).

Available in powder form and in tablets of 0.25 g, as well as in compound tablets containing theobromine with phenobarbital, salsoline, papaverine and other spasmolytics, sedatives and hypnotics.

To be kept in well closed bottles in a place protected from light, observing safety precautions (List B).

THEOBROMINE SODIUM SALICYLATE (*Theobrominum natrium et Natrii salicylas*)



Synonyms Azurin Diuretin Nocthylline Theosin

White powder very freely soluble in water The 10% aqueous solution is alkaline to phenolphthalein Absorbs carbon dioxide from the air Hygroscopic Solutions are incompatible with acids and carbonates

Solutions are prepared aseptically or are Tyndallized 3 times at 96°

Has a diuretic and vasodilator effect has little influence on the central nervous system

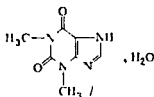
Used orally in coronary insufficiency hypertensive disease and edema of cardiac and renal origin

Adults are prescribed doses of 0.3-0.5 or 0.75 g Children up to 1 year old — 0.03—0.05 g 2—5 years — 0.1—0.2 6—12 years — 0.2—0.4 g

Available in powder form To be kept in well closed bottles in a dry place On being moistened theobromine sodium salicylate is decomposed into sodium theobromine and sodium salicylate In compound drugs theobromine sodium salicylate is replaced by equivalent amounts of theobromine and sodium salicylate

Theobromine sodium salicylate is chiefly prescribed in mixtures or powders which should not be stored for lengthy periods

THEOPHYLLINE (Theophyllinum) 1.3 Dimethylxanthine



Synonym Theocin

Alkaloid contained in tea leaves and coffee Now being produced synthetically White crystalline powder odourless sparingly soluble in cold water (1:180) more soluble in hot water (1:85) freely soluble in acids and alkalis Melting point 268—272°

Similar in pharmacological effect to other alkaloids of the purine series particularly theobromine Is distinguished by a more pronounced diuretic effect Strongly dilates the vessels of the heart also dilates the bronchial muscles. Stimulates the central nervous system

Mainly employed as a diuretic in congested conditions of cardiac and renal origin and likewise as a vasodilator in coronary insufficiency

Administered orally in a dosage of 0.1—0.2 g 3—4 times a day A good effect is also observed when the drug is administered in the form of suppositories

Maximal doses for adults single—0.4 g daily—1.2 g

Maximal doses for children 2 years single—0.04 g daily—0.12 g 3—4 years single—0.05 g daily—0.15 g 5—6 years single—0.06 g daily—0.2 g 7—9 years single—0.08 g daily—0.25 g 10—14 years single—0.1 g daily—0.3 g Children up to 2 years old are not prescribed theophylline

Side effects are sometimes observed when theophylline is used heartburn nausea vomiting diarrhea headache

In cases of overdosage epileptoid attacks may develop In order to prevent side effects involving the central nervous system it is recommended that theophylline should not be taken for more than two or three days in succession

Available in powder form

To be stored in tightly closed bottles of dark glass observing safety precautions (List B)

Theophylline is the basic constituent of aminophylline. It is also an ingredient of theophedrine.

Theophedrine (Theophedrinum) Tablets containing 0.05 g theophylline, 0.05 g theobromine, 0.05 g caffeine, 0.2 g aminopyrine, 0.2 g phenacetin, 0.02 g ephedrine hydrochloride, 0.02 g phenobarbital, 0.02 g powdered Belladonna leaf, 0.0002 g lobeline hydrochloride or 0.0001 g cytisine.

Used as a therapeutic and prophylactic agent in bronchial asthma. Adults are prescribed $\frac{1}{2}$ —1 tablet once a day (2 tablets in severe attacks). Children from 2 to 5 years old are prescribed $\frac{1}{4}$ — $\frac{1}{2}$ tablet, from 6 to 12 years — $\frac{1}{2}$ — $\frac{3}{4}$ tablet. In order to avoid disturbed sleep at night, theophedrine should be taken in the morning or daytime. Maximal daily dose for adults — 2 tablets.

Antasthman (Antasthman) Tablets containing 0.1 g theophylline, 0.05 g caffeine, 0.2 g aminopyrine, 0.2 g phenacetin, 0.02 g ephedrine hydrochloride, 0.02 g phenobarbital, 0.01 g Belladonna extract, 0.09 g powdered Lobelia leaf.

Used like theophedrine for the treatment and prevention of attacks of bronchial asthma. The method of administration and the dosage are the same as for theophedrine.

The drug is manufactured in the Czechoslovak Socialist Republic and has been approved for use in the USSR.

AMINOPHYLLINE (Aminophyllinum)

Double salt of theophylline and ethylenediamine. Contains approximately 80% theophylline.

Synonyms: Aminocardol, Aminomed, Aminophyllin, Carena, Diaphyllin, Euphylline, Genophyllin, Inophylline, Metaphyllin, Neophyllin, Theolamine, Theophyllidine, Theophyllamin, Theophylline ethylenediamine.

White (or white with a yellowish tint) crystalline powder with faint odour of ammonia, freely soluble in water. Aqueous solutions have an alkaline reaction. Has a vasodilator and diuretic effect, increases the excretion of chlorides in the urine. Strongly dilates the coronary vessels and has a particularly pronounced effect in relaxing the smooth muscles of the bronchi; stimulates myocardial contractions.

Employed in bronchial asthma, in angina pectoris with symptoms of congestive cardiac insufficiency, especially in cardiac asthma and in other diseases of the heart accompanied by congestive symptoms. It has been reported that aminophylline is one of the most effective contemporary agents in the treatment of cardiac asthma, particularly when attacks are accompanied by marked bronchospasms or impairment of respiration of the Cheyne Stokes type (A. I. Kuseyev, A. V. Meshcheryakova, M. Y. Slutsky et al.).

Aminophylline is likewise effective in apoplexy; intravenous administration at the beginning of apoplexy may halt it or lighten the course (L. G. Chilenov, Y. N. Zakharova).

Aminophylline is prescribed orally, intramuscularly and intravenously as well as in the form of rectal suppositories and in micro-enemas. Aminophylline solutions are not injected subcutaneously as they have an irritating effect on the tissues.

The method of administration depends on the peculiarities of the case; in acute attacks of cardiac or bronchial asthma, in apoplexy and the like, the drug is given intravenously; in other cases the oral or some other method is used.

Orally, aminophylline is taken in doses of 0.1—0.2 g, 2—3 times a day after meals (in tablets or capsules).

Intramuscularly, 2—3 ml 12% solution (0.24—0.36 g aminophylline) is injected.

For intravenous administration 5—10 ml 24% aminophylline solution is diluted with 10—20 ml 20% or 40% glucose solution; the injection is given slowly (over a period of 4—6 min). Intravenous administration is also possible by the drip method (0.24—0.48 g aminophylline in 500 ml 5% glucose solution is infused over a period of 2—2½ hours).

Suppositories containing 0.2–0.4 g aminophylline are used for rectal administration for microcnemas 0.3–0.5 g of the drug is dissolved in 20–25 ml warm water

Aminophylline can be prescribed in combination with other drugs: cardiac spasmolytics, sedatives, etc.

Maximal doses for adults orally, single — 0.5 g daily — 1.5 g intramuscularly and intravenously single — 0.25 g daily — 0.5 g

When aminophylline is taken orally dyspeptic symptoms associated with its irritating effect are possible. When rapidly injected intravenously the following side effects may be observed: vertigo, headache, palpitation, nausea, emesis, convulsions, marked lowering of the arterial pressure.

When administered rectally irritation of the mucous membrane of the rectum may be observed.

The use of aminophylline, particularly intravenous administration, is contraindicated in acute cases of myocardial infarction with abrupt lowering of the arterial pressure, pronounced coronary sclerosis, instability of the autonomic nervous system, as well as paroxysmal tachycardia and extrasystole. Aminophylline should not be administered intravenously to children up to 14 years old.

Available in powder form in tablets of 0.1 g in ampoules containing 2 ml 12% solution for intramuscular administration and in ampoules containing 10 ml 2.4% solution for intravenous injections. Ampoules containing 12% solution can likewise be used for intravenous administration when properly diluted (2 ml 12% solution is diluted with 20 ml 20% or 40% glucose solution).

To be stored in a place protected from light, observing safety precautions (List B).

Rp Aminophyllini

Amobarbitali natrici 33 0.25

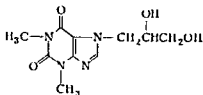
Butyri Cacao 15

M f suppos D t d N 6

S 1 suppository twice a day

DIPROPHYLLINE (Diprophyllum)

7 (2,3 dihydroxypropyl) theophylline



Synonyms: Aristophyllin, Astrophyllin, Coronal, Coronarin, Corphyllamin, Neutral Didrofillina, Diprophyllin, Dyphylline, Glyfyllin, Glyphyllin, Isophyllin, Neutraphyllin, Silbephylline, Solufyllin, Teofene, Thefylan.

White crystalline powder, freely soluble in water. Melting point 159.5–160.5°.

Diprophylline is similar to theophylline and aminophylline in pharmacological properties: dilates the coronary vessels and the bronchi, somewhat increases uric acid excretion, has no marked stimulating effect on the central nervous system. The high solubility in water makes it possible to administer diprophylline not only orally but parenterally as well. Less toxic than theophylline. Has a stronger effect than aminophylline but is less toxic and does not irritate the tissues.

Diprophylline is employed in spasms of the coronary vessels, cardiac and bronchial asthma and hypertensive disease. Prescribed orally, intravenously, intramuscularly and rectally. It can abort or prevent attacks of the disease depending on the method of administration. Intravenously, adults are usually given injections of 10 ml 2.5% solution once or twice a day, intramuscularly

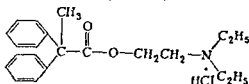
the dose is 3—5 ml 10% solution Orally 0.25—0.5 g is prescribed 3—4 times a day In suppositories 0.5 g is administered

Safety precautions are to be observed in storage

D Esters of carbonic acids

APROPHEN (Aprophenum)

β Diethylaminoethyl diphenylpropionate hydrochloride



White crystalline powder freely soluble in water alcohol chloroform sparingly soluble in acetone and benzene very slightly soluble in ether Melting point 161—165° Aqueous solutions are stable when neutral but are hydrolyzed when alkaline they are sterilized by holding at 100° for 30 min

Related in chemical structure and similar in pharmacological properties to spasmolytin (see p 104) differs from the latter in having a CH_3 group attached to the carbon atom in the α position to the carboxyl group instead of in atom of hydrogen

Aprophen has a marked spasmolytic and vasodilator effect it strongly dilates the coronary vessels being considerably more potent in this respect than spasmolytin and papaverine it is likewise more potent than spasmolytin in its peripheral cholinolytic effect

Aprophen also causes a raising of the tone of the uterus and an intensification of uterine contractions

Aprophen is used as a spasmolytic in spasms of the vessels (spasms of the cerebral vessels endarteritis and particularly spasms of the coronary vessels) and in spasms of the abdominal organs (spastic colitis cholecystitis renal and hepatic colic ulcer) as well as in menorrhagia it is also used to stimulate labour

While intensifying uterine contractions aprophen simultaneously diminishes cervical spasm and promotes more rapid dilation of the cervix in the first stage of labour

Prescribed orally in a dosage of 0.025 g 2—4 times a day after meals subcutaneously or intramuscularly 0.5—1 ml 1% solution is injected

Maximal doses for adults single—0.03 g daily—0.1 g

The course of treatment is for 10—15 days

In order to stimulate labour 1 ml 1% aprophen solution can also be injected into the tissue of the cervix

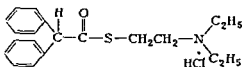
As a consequence of aprophen's atropine like action it may cause dryness in the mouth acceleration of the pulse and dilation of the pupils At times when the drug is taken there may be vertigo a peculiar feeling of intoxication nausea and a burning sensation in the epigastric region

Available in powder form and in tablets of 0.025 g

To be stored in a place protected from light observing safety precautions (List B)

TIPHEN (Tiphenum)

β Diethylaminoethyl thiophenylacetate hydrochloride



Synonym Trocinate

White crystalline powder odour resembling that of mercaptan characteristic soluble in water freely soluble in alcohol very slightly soluble in ether melting point 123—130° Solutions for injection are prepared ex tempore in aseptic conditions on standing they are hydrolyzed and become turbid

In chemical structure tiphens is closely related to spasmolytin of which it is a sulphur containing analogue a derivative of thiodiphenyl acetic acid

Tiphens has a more pronounced spasmolytic and vasodilator effect than spasmolytin and has less influence on the central nervous system It is superior to papaverine in spasmolytic potency Also has an atropine like and local anesthetic effect

Used in spasms of the blood vessels stenocardia headache associated with muscular spasm hypertensive disease of I and II degree spasms of the abdominal organs cholecystitis ulcer colitis renal colic etc also used in bronchial asthma

Prescribed orally in tablets after meals Adults are given 0.03 0.05 or 0.1 g 2—3 times a day older children are given 0.01—0.015 g 2—3 times a day

Maximal doses for adults single—0.1 g daily—0.3 g
Tiphens can be used in combination with other drugs phenobarbital theobromine sodium salicylate papaverine promedol phenadone etc

Subcutaneously injections of 1 ml 0.5% or 1% solution are given After using the powder there may be a transitory numbness in the mouth as a consequence of the drug's local anesthetic properties

When working with tiphens measures must be taken to prevent it coming into contact with the skin and mucous membranes since repeated exposure may cause symptoms of irritation

Because of tiphens irritant effect which makes it difficult to prepare powders it is recommended that the drug be prescribed in tablets When using tiphens in combination with other drugs it is also recommended that the drug should be prescribed in tablets in addition to the other ingredients

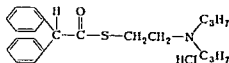
Available in powder form and in tablets of 0.02 and 0.03 g

To be kept in amber bottles with ground glass stoppers observing safety precautions (List B)

Rp Tiphens 0.02 (0.03)
D 1 d N 10 in tabul
S 1 tablet 2—3 times a day

DIPROPHEN (Diprophenum)

β Di n propylaminoethyl thiodiphenylacetate hydrochloride



White crystalline powder of bitter taste soluble in water (1:100) on heating slightly or on the addition of 1—2 drops 1 N hydrochloric acid Melting point 132—134°

Closely related in chemical structure and similar in pharmacological properties to tiphens differs from the latter in having two n propyl groups ($\text{CH}_2\text{CH}_2\text{CH}_3$) attached to the nitrogen atom of the side chain instead of ethyl groups (CH_2CH_3) Less toxic than tiphens and less irritating while having a more pronounced vasodilator effect Inferior to tiphens in cholinolytic potency

Used as a spasmolytic in spasms of the blood vessels Especially effective in spasms of the vessels of the extremities (endarteritis Raynaud's disease)

etc.) Likewise employed in spasms of the smooth muscles of the internal organs (spasms of the stomach intestine urinary tract and bronchi)

Prescribed orally in a dosage of 0.025–0.05 g, 2–3 times a day. If tolerated well the single dose may be increased to 0.1 g. The spasmolytic effect develops gradually. The effect in endarteritis (abatement of pain, improvement of the circulation, etc.) is usually observed on the 5th to 7th day of treatment. The course of treatment lasts 15–20 days. If necessary treatment may be repeated.

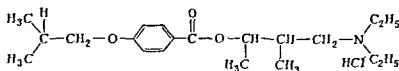
The drug is usually tolerated well. In individual cases vertigo, headache and nausea are observed. As a consequence of the local anesthetic effect there may be a feeling of numbness in the mouth, particularly when the drug is taken in powder form.

Available in powder form and in tablets of 0.025 and 0.05 g.

To be stored in a dry place protected from light, observing safety precautions (List B).

Gangleron (Gangleronum)

α , β Dimethyl γ diethylaminopropyl p isobutoxybenzoate hydrochloride



Colourless crystalline powder. Freely soluble in water, hygroscopic. Solutions are sterilized by holding at 100° for 30 min.

Has a cholinolytic, spasmolytic and local anesthetic effect.

Blocks the n cholinoreactive systems of the autonomic ganglia (sympathetic and parasympathetic) and the central nervous system, but has no influence on the m cholinoreactive systems. Causes relaxation of the smooth muscles and dilation of the blood vessels.

Gangleron can be used as a spasmolytic in various pathological conditions accompanied by spasms of the smooth muscles. Its effect in stenocardia has been investigated more fully than in other diseases.

The drug is mainly employed to prevent attacks of stenocardia.

Administered by mouth, subcutaneously and intramuscularly. It is not injected intravenously as there may be an abrupt lowering of the arterial pressure.

In moderate and severe forms of stenocardia (with frequent attacks of angiospasm) the drug is prescribed 4 times a day and in mild forms 3 times a day, according to the following schedule: 1st and 2nd day — 1.5 ml 1.5% solution intramuscularly or subcutaneously; 3rd and 4th day — 2 ml; from 5th to 10th day — 3 ml. Beginning with the 10th day one injection is replaced by oral administration of 1 teaspoonful of 1.5% solution diluted with 50–75 ml water (to be taken before meals) over a period of 4 days. Injections are fully replaced by oral administration. The drug is also given in tablets of 0.04 g. The entire course of treatment lasts 4–5 weeks (on an inpatient basis).

If the effect is not sufficiently pronounced by the 7th–9th day, an additional intradermal block is produced instead of an injection or oral administration of the drug. An intradermal block is instituted using a 0.2–0.25% solution; the next day a bilateral paravertebral block is instituted at the D_1 – D_2 level.

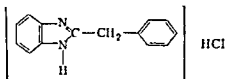
Gangleron is usually tolerated well. On coming into contact with the tongue it causes a sensation of slight irritation with subsequent anesthesia. The drug cannot be used for injections in a concentration higher than 1.5% since it may cause irritation and necrosis of the tissues.

Available in powder form in ampoules containing 2 ml 15% solution in tablets of 0.01 g and in vials containing 100 ml 15% solution for oral administration

E Various synthetic compounds and drugs of the natural origin

DIBAZOL (Dibazolum)

2-Benzylbenzimidazole hydrochloride



White crystalline powder with pale yellowish or greyish tint bitter salty taste freely soluble in hot water sparingly soluble in cold freely soluble in alcohol insoluble in ether Melting point 182—186° Solutions have an acid reaction and should be used warm since soon after cooling dibazol begins to crystallize out Solutions are prepared in aseptic conditions

Dibazol has a vasodilator spasmolytic and hypotensive effect, it also has a stimulating influence on the functions of the spinal cord

Used in spasms of the blood vessels (coronary insufficiency hypertensive crises) and spasms of the smooth muscles of the internal organs (ulcer of the stomach pylorospasm intestinal spasm etc) as well as in the treatment of nervous diseases for the most part sequelae of poliomyelitis peripheral paralysis of the facial nerve etc

As a spasmolytic dibazol is prescribed orally or subcutaneously Dosage for adults orally — 0.02 g 3 times a day or 0.05 g twice a day subcutaneously — 1—2 ml 1—2% solution once a day Course of treatment 10—30 days

In hypertensive crises 1—2 ml 1% solution is given intravenously up to 3—4 times a day

In the treatment of nervous diseases dibazol is administered from 5 to 10 times in a dose of 0.005 g (for adults) one powder a day or one powder each second day In 3—4 weeks the course of treatment is repeated Subsequent courses are given at intervals of 1—2 months

Maximal doses for adults single — 0.05 g daily — 0.15 g

Children are prescribed dibazol in the following doses for the treatment of diseases of the nervous system up to 1 year old — 0.001 g 1—3 years — 0.002 g 4—7 years — 0.003 g 8—12 years — 0.004 g over 12 years — 0.005 g

Maximal doses for children (single and daily) up to 6 months old — 0.001 g from 6 months to 1 year — 0.001 g 2 years — 0.002 g 3—4 years — 0.004 g 5—6 years — 0.005 g 7—9 years — 0.006 g 10—14 years — 0.008 g

Dibazol is to be taken 2 hours before or 2 hours after meals

Available in powder form and in tablets Is also an ingredient of compound tablets (see Phenobarbital Papaverine Theobromine)

Safety precautions are to be observed during storage (List B)

TRIACANTHINE HYDROCHLORIDE (Triacanthinum hydrochloricum)

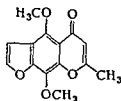
Hydrochloride of an alkaloid (C₁₀H₁₃N₅ HCl) isolated from the leaves of the Common Honeylocust (Gleditsia triacanthos L.) family Leguminosae which grows in the southern regions of the USSR

White crystalline powder soluble in water Melting point 219—220°

Has a papaverine like effect Prescribed orally in a dose of 0.1 g 2—3 times a day before meals in spasms of the intestine and bronchial asthma

KHELLIN (Khellinum)

Obtained from seeds of *Ammi visnaga* L. which is cultivated in the USSR
2 Methyl 5,8 dimethoxy 6,7 furanochromone



Synonyms Amicardin Amikhelline Ammivin Benecardin Chellin Khellinorm Visammun

White crystalline powder odourless bitter taste sparingly soluble in cold water more soluble in hot freely soluble in alcohol acetic acid 25% sodium salicylate solution and saturated sodium benzoate solution Melting point 152—154°

Khellin has a spasmolytic effect it dilates the coronary arteries bronchi and smooth muscles of the abdominal organs also has a moderate sedative effect According to information in the literature the drug has a favourable influence on the oxidation reduction system of the myocardium

Khellin is mainly used in the treatment of patients with stenocardia and bronchial asthma It is prescribed for the prevention of attacks since it has no abortive effect In acute attacks of stenocardia nitroglycerol or other drugs are given in attacks of bronchial asthma — adrenalin ephedrine or other drugs When the attack has been aborted khellin is administered

Single dose 0.02 g (at times 0.04 g) Prescribed orally 3—4 times a day after meals In stenocardia the course of treatment is for 2—3 weeks A therapeutic effect is usually observed in 5—7 days If necessary the course of treatment can be repeated

Maximal doses for adults single—0.04 g daily—0.12 g

Khellin is contraindicated in pronounced symptoms of insufficiency of the circulation In individual patients nausea vomiting or deterioration in subjective feeling may be observed when the dose is lowered these symptoms usually pass away

Available in tablets of 0.02 g

To be stored in a dry place protected from light observing safety precautions (List B)

Rp Khellini 0.02

D t d N 25 in tabul

S 1—2 tablets 2—3 times a day

DAUCARIN (Daucarinum)

Extract of the seeds of the Carrot (*Daucus carota* or *D. sativus* (Hoffm.) Roehl) Parsley family (Umbelliferae)

Yellow brown amorphous powder of bitter taste Forms a turbid solution with water (1%) soluble in 50° alcohol

Has a spasmolytic effect similar to khellin in pharmacological properties

Used in chronic coronary insufficiency The effect develops gradually side effects are usually not observed

Administered orally in a dose of 0.02 g 3—5 times a day (30 min before meals) Course of treatment 2—4 weeks

Available in tablets of 0.02 g

To be stored in a place protected from light (observing safety precautions (List B)

Rp Daucarini 0.02

D t d N 20 in tabul

S 1 tablet 3 times a day (30 min before meals)

EUCOMMIA BARK (Cortex Eucommiae)

The bark of *Eucommia ulmoides* Oliv. a bush of the Elm family, low growing in Abkhazia. Contains milk sap, guttapercha and other substances. Extracts and tinctures of the bark cause a lowering of the arterial pressure.

Administered orally in hypertensive disease in the form of an infusion, fluid extract or tincture (20% tincture made with 30° alcohol), in a dosage 15—20 drops 2—3 times a day.

Rp Extr. fluidi Eucommiae 250
DS 15—30 drops 2—3 times a day
Rp T. rac. Eucommiae 150
DS 15—30 drops 2—3 times a day

BAIKAL SKULLCAP RHIZOME (Rhizoma Scutellariae)

Rhizomes of the Baikal Skullcap (*Scutellaria baicalensis* Georgi), Malvaceae family (Labiales).

Habitat Trans-Baikal region and Eastern Siberia. Contains tannin of the pyrocatechol group, the glycoside scutellarin, volatile oil and other substances. It is a hypotensive and sedative effect.

A tincture of the rhizome has been proposed for the treatment of hypertensive disease. It improves patients' subjective condition and in early stages causes a lowering of the arterial pressure. The tincture (20% tincture made with 70° alcohol) is a transparent reddish-brown liquid with characteristic odor and bitter taste.

Prescribed orally 20—30 drops 2—3 times a day.

To be stored in a place protected from light.

CIMICIFUGA TINCTURE (Tinctura Cimicifugae dahuricae)

20% tincture (made with 70° alcohol) of the roots of *Cimicifuga dahurica* Maxim. habitat Ussuri Territory.

Transparent light brown liquid with aromatic odor and bitter taste.

Used as a sedative and hypotensive agent in the early stages of hypertensive disease.

Prescribed orally 50—60 drops 2—3 times a day.

SOUTHERN MAGNOLIA (Magnolia grandiflora)

An alcoholic fluid extract of the leaves is used. Transparent dark cherry-red liquid with bitter burning taste. Contains alkaloids (0.14%), glycosides (0.14%), volatile oils and extractives. Prescribed orally 20—30 drops 3 times a day in the early stages of hypertensive disease. Course of treatment 3—4 weeks.

OMELEN (Omelenum)

Thick extract of the leaves of the White Mistletoe (*Viscum album* L.) family Loranthaceae, parasitic on the poplar.

Thick dark brown mass with specific odor and bitter taste, soluble in water.

Used in the early stages of hypertensive disease. 0.2 g in tablets or 20—40 drops of 10% solution 3 times a day.

DOWNY FLOWERED ASTRAGALUS

Downy flowered *Astragalus* (*Astragalus pubiflorus*) family Leguminosae habitat—Crimea, Black Sea coast, lower Don region, as well as other places. Infusions have a sedative effect, cause a dilation of the blood vessels and lowering of arterial pressure and increase diuresis.

Has been proposed for use in hypertensive disease, stenocardia and cardiovascular insufficiency with symptoms of congestion.

Prescribed in the form of an infusion (1:10), 1—2 tablespoonfuls 3—4 times a day or in enemas of 50 ml twice a day.

BOG GNAPHALIUM (Gnaphalium uliginosum)

Annual family Compositae, which grows mostly in the central part of the USSR in Europe in moist meadows and along the banks of rivers. The leaves and roots gathered when flowering are used (*Herba cum radix Gnaph.*

uliginosi) Contains carotene, vitamin C, the alkaloid gnaphaline, resin, tannin, colouring matter and other substances

Gnaphalium preparations slightly dilate the blood vessels and cause some lowering of the blood pressure. Oil extracts of the herb somewhat stimulate granulation and epithelization of injured tissues

Gnaphalium is chiefly used at present in the treatment of patients with ulcer of the stomach, slow healing wounds, ulcers and burns, less often used in treating patients with light forms of hypertensive disease

LIME FLOWERS (Flos Tiliae)

Dried entire cymes with bracts of the Small leaved Lime (*Tilia cordata* Mill) and the Large leaved Lime (*Tilia platyphyllos* Scop), family Tiliaceae, gathered when fully expanded

Contain volatile oil, a glycoside, tannin, mucilage and other substances

1—2 glassfuls of an infusion are administered orally as a sudorific (a table spoonful of finely cut flowers is steeped in a glassful of boiling water, let stand 20 min and filtered). The infusion is also used for rinsing the mouth and pharynx. Is an ingredient of sudorific tea number 1

The mechanism of the sudorific action of Lime flowers and other sudorifics has not been investigated sufficiently. It is assumed that along with the influence on the cells of the sweat glands, the substances contained in the plants used for this purpose cause a dilation of the blood vessels supplying these glands. The sudorific effect is promoted by drinking large amounts of warm liquids

ANGIOTROPHIN (Angiotrophinum)

An aqueous extract of the pancreas freed of insulin (similar to *Padutin* or *Kallikrein*). Colourless transparent liquid. Has the ability of enlarging the blood vessels and lowering the arterial pressure

Used in spastic forms of endarteritis, Raynaud's disease, stenocardia, migraine, the early stages of hypertensive disease etc

Administered subcutaneously or intramuscularly in doses of 1 ml. Course of treatment 5—10 days

Available in ampoules of 1 ml

To be stored in sealed ampoules in a dark place

Chapter V

DIURETICS

Diuretics are substances which stimulate the flow of urine and bring about a reduction in the content of fluid in the interstitial tissue and the serous cavities. The action of most modern diuretics is based on their ability to increase the excretion of the salt ions contained in the extracellular fluid, the cation Na^+ and the anions Cl^- or HCO_3^- ; this in turn leads to the excretion of corresponding amounts of water.

The term "saluretics" is now being used in the literature along with that of diuretics; the former term is applied to substances which promote a particularly intense excretion of sodium and chlorine ions.

Diuretics are used for the most part in diseases of the heart, liver and kidneys accompanied by edema.

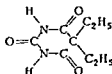
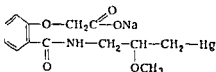
Diuretics should be looked on as auxiliary agents which promote an abatement or disappearance of congestive symptoms; attention during treatment should primarily be directed toward eliminating the pathological process causing the accumulation of fluid in the body.

During recent years a number of new effective diuretics have been synthesized. Along with the mercury diuretics, the xanthine derivatives and the like, formerly used inhibitors of carbonic anhydrase, pyrimidine derivatives, chlorothiazide and its analogues, etc., today find wide application in medical practice.

I MERCURY DIURETICS

MERCUSAL (Mercusalum)

10% aqueous solution of the sodium salt of salicyl (3-hydroxymercuri-2-methoxypropyl) amide acetic acid combined with barbital in equimolecular proportions.



Colourless or slightly coloured transparent liquid of alkaline reaction. Contains approximately 4% mercury.

Mercusal is an extremely effective mercurio-organic diuretic. According to modern conceptions its diuretic action, like that of other mercury diuretics, can

be ascribed to its ability to block the renal enzymes that ensure the transport of electrolytes in the first place the sulfhydryl groups of succinate dehydrogenase are blocked forming inactive mercaptides. The depression of reabsorption in the proximal tubules leads to a considerable increase in the excretion of sodium ions and a still greater increase in the excretion of chlorine. The excretion of potassium also rises while diuresis mounts sharply. It is possible that the reduction in the hydrophilic property of the tissues and its influence on the neural apparatus of the kidneys play a certain role in the diuretic action of mercusol.

When mercusol is administered the diuretic effect usually begins in 2—3 hours, reaches the maximum in 4—6 hours and continues for 24 hours or more.

Indications for the use of mercusol: 1) chronic cardiac insufficiency accompanied by edema, ascites, hydrothorax, congestive manifestations in the lungs and liver, etc. 2) cirrhosis of the liver accompanied by congestion in the system of the portal vein. 3) lypoid and amyloid — lypoid nephrosis with a pronounced edematous syndrome. 4) venous congestion arising from pressure on the great veins (tumours of the mediastinum, etc.).

Mercusol has a relatively high toxicity and therefore it should only be employed in cases where other diuretics do not give the desired effect. Administration is permissible only after an examination of the urine in order to exclude the possibility of kidney diseases marked by impairment of the concentrating ability of the kidneys.

Mercusol is administered intramuscularly (in the outer upper quadrant of the buttocks).

Adults are usually prescribed 0.5—1 ml every 4—5 days, sometimes small doses (0.25—0.3 ml) are given daily for 4—5 days or each second day for 8—10 days.

Maximal dose (single and daily) intramuscularly for adults 1 ml.

Maximal dose (single and daily) intramuscularly for children up to 6 months old — 0.1 ml, from 6 months to 1 year — 0.15 ml, 2 years — 0.2 ml, 3—4 years — 0.25 ml, 5—6 years — 0.4 ml, 7—9 years — 0.6 ml, 10—14 years — 0.7 ml.

When injecting mercusol into the muscle it is recommended that the needle should be changed after the solution has been drawn into the syringe from the ampoule in order to prevent the drug from coming under the skin. Care must also be taken that no alcohol is left in the syringe or needle. Mercusol is not administered subcutaneously since such injections are painful and may lead to the development of local necrosis. The drug is administered in the morning so as not to disturb the patient's sleep at night and so that the physician can observe the development of the diuretic effect. Measurement and analysis of the diurnal urine after each administration of mercusol is obligatory.

Calcium chloride or ammonium chloride (see pp. 188, 297) are often prescribed in order to heighten the diuretic effect of mercusol. Ammonium chloride is given orally in capsules 1—2 g 5 times a day or in the form of an aqueous solution (the daily dose in 150—200 ml water).

It should be borne in mind that lengthy therapy with mercury diuretics sometimes leads to the development of hypochloremic alkalosis which lowers the effectiveness of treatment. In such cases it is also expedient to prescribe ammonium chloride.

In congestive manifestations associated with impairment of cardiac activity it is advisable to combine mercusol treatment with the administration of cardiotonics (the preliminary prescription of Foxglove preparations or the simultaneous administration of strophanthin). Caution must be observed when using mercusol for patients who are taking Foxglove preparations since during diuresis accompanied by the intensified excretion of potassium the sensitivity of the heart to cardiac glycosides rises and symptoms of Foxglove intoxication may develop. In cases of necessity potassium chloride is prescribed.

Reports have recently appeared in the literature on the use of mercusol for the treatment of serious forms of psoriasis (M. I. Per et al.). The authors

observed a favourable effect when the drug was administered intramuscularly in doses of 1-1.5 or 2 ml twice a week the course totalled 12-14 injections. It should be noted that these doses are in excess of those used for achieving a diuretic effect and that they can be given only when there are no contra-indications and on condition that an especially close watch is kept on the patient's general condition and the function of the kidneys.

When mercusol is used, there may be various side effects associated with the drug's local irritant properties and general toxic action on the body.

Local symptoms of irritation are particularly pronounced when the drug is administered subcutaneously but even when given intramuscularly there may be pain, irritation and an inflammatory reaction at the site of injection.

At the beginning of treatment with mercusol it must be ascertained whether or not the patient has a heightened sensitivity to the drug. Sometimes after the first injection (not more than 0.5 ml should be injected) there may be profuse sweating, watery stool, weakness and pain in the extremities. During treatment watch must be kept for the possible development of mercury intoxication. If there should be pyralism, dyspeptic symptoms, the appearance of blood in the excrement or other complications, a break must be made in injections or the drug withdrawn completely. It must be remembered that when mercusol has a toxic effect there may be serious affections of the kidneys.

Cases of pronounced symptoms of mercusol intoxication call for the administration of unithiol or other drugs such as dimercaptopropanol which contain active sulphhydryl groups. By restoring the activity of the thiol groups of the enzymes that have been blocked by mercury, unithiol diminishes the toxic action of mercusol; the diuretic effect thereupon ceases.

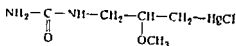
Contraindications to the use of mercusol: 1) vascular affections of the kidneys, acute and chronic nephritis, nephrosclerosis, amyloid shrivelled kidney, etc. 2) insufficient concentrating ability of the kidneys (sp. gr. of the urine below 1.018-1.020). 3) absence of a marked increase in the amount of urine after the first or some subsequent administration of mercusol. 4) acute impairment of the function of the intestine (diarrhoea).

Available in ampoules containing 1 ml.

To be stored in sealed ampoules observing safety precautions (List B).

PROMERAN (Promeranium)

3 Chloromercuri 2 methoxypropylurea



Synonyms: Chloromerodrin, Mercioran, Mercurylurée, Merilid, Merparan, Neohydryn, Oricur, Percapyl.

White crystalline powder, bitter (metallic) taste, soluble in water and alcohol. Melting point 152-153°. Contains 51.6% mercury.

Mercury diuretic with marked effect when administered orally, the mode of action is fundamentally analogous to that of mercusol.

Used in congestive manifestations in patients with insufficiency of the circulation and in affections of the liver, as well as in lipid and amyloid lipid nephroses when the functional ability of the kidneys has been preserved.

In some cases promeran can fully replace injections of mercusol, the two drugs can also be used together making it possible considerably to reduce the number of injections of mercusol.

In pronounced ascites and in cases of impairment of the process of absorption in the gastrointestinal tract it is expedient to begin treatment with intramuscular injections of mercusol and then go over to the administration of promeran.

Promeran is taken orally in tablets each tablet contains about 18 mg of the drug the equivalent of 10 mg of mercury. Doses should be individualized depending on how serious the disease is and how well the drug is tolerated. Usually one tablet is prescribed 3—4 times a day after meals. In more serious cases large doses are prescribed the first few days up to 6—8 tablets daily. When a marked diuretic effect is achieved the dose is reduced to 3 or 4 tablets a day. Children are given smaller doses according to their age. It is recommended that a 3—4 day break in treatment should be made after every 4—5 days administration of the drug since the diuretic effect declines during lengthy uninterrupted treatment.

The diuretic effect usually begins to appear on the second day of treatment and reaches the maximum on the 3rd or 4th day the effect persists for several days after the drug is withdrawn.

The effect of promeran (like that of mercusol) can be intensified by the simultaneous oral administration of ammonium or calcium chloride.

Dyspeptic symptoms headache and pruritus are observed at times when using promeran. Gingivitis and stomatitis seldom occur as symptoms of mercury poisoning.

Treatment with promeran requires careful observation of the patient's condition. If there is no marked diuretic effect the drug is withdrawn. The appearance of symptoms of intoxication such as diarrhea and other dyspeptic manifestations and irritation of the kidneys likewise makes it necessary to withdraw the drug or make a break in treatment.

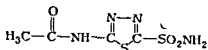
Contraindications are the same as for mercusol.

To be kept locked (List A) in tightly closed bottles in a place protected from light.

II CARBONIC ANHYDRASE INHIBITORS

ACETAZOLAMIDE (Acetazolamidum)

2 Acetyl amino 1 3 4 thiadiazole-5 sulfamide



Synonyms Diacarb Diamox Diluran Diuramid Fonurit Nephramid Renamid Sulfadiurine

White crystalline powder sparingly soluble in water. Melting point 258—260°.

Acetazolamide is one of a new group of drugs whose use is based on their selective ability to inhibit carbonic anhydrase—an enzyme involved in the hydration and dehydration of carbonic acid. This property was first discovered in sulfanilamide and other sulfonamides but it is considerably more pronounced in acetazolamide.

Acetazolamide can be used for medicinal purposes in the presence of various indications making it desirable to lower the activity of carbonic anhydrase. The greatest application today is as a diuretic as well as in the treatment of glaucoma.

The diuretic effect is based on the inhibition of carbonic anhydrase in the kidneys and the resulting shift in the alkaline equilibrium in the body. The inhibition of carbonic anhydrase causes a reduction in the amount of carbonic acid formed in the kidneys and a diminution of the reabsorption of bicarbonate by the epithelium of the tubules. The amount of Na and HCO₃ ions excreted in the urine rises and at the same time the excretion of water also increases con-

siderably the pH of the urine rises. The excretion of K ions likewise increases under the influence of acetazolamide. There is no increase in the excretion of chlorides.

As a result of the intensified excretion of bicarbonate the alkaline reserve of the blood falls and acidosis may develop.

The alkaline reserve returns to the initial value in 1—2 days after the administration of acetazolamide is discontinued.

Acetazolamide is effective when taken orally. It is quickly absorbed from the gastrointestinal tract and entering the tissues and organs inhibits the carbonic anhydrase they contain.

As a diuretic acetazolamide is mainly used in edema of cardiac origin; it is also effective in nephroses and in cirrhosis of the liver.

Acetazolamide is likewise used in treating glaucoma in different phases of development and degrees of compensation (in simple congestive, juvenile and other forms of primary and secondary glaucoma). The lowering of intraocular pressure brought about by the drug is associated with inhibition of the carbonic anhydrase of the ciliary body and reduced secretion of chamber fluid. Acetazolamide, unlike miotics, does not cause contraction of the pupil and an intensification of the outflow of chamber fluid. Inasmuch as acetazolamide does not cause contraction of the pupil, it can be used in the presence of cataract. The most pronounced hypotensive effect is observed in patients with an acute attack of glaucoma.

The use of acetazolamide creates favourable conditions for surgical intervention in glaucoma. Its administration in the preoperative period reduces the likelihood of complications, while its use in the postoperative period improves the course (N. A. Pletnyova and S. M. Sakhieva).

Acetazolamide is also used in the treatment of epilepsy. It is possible that the therapeutic effect is associated with inhibition of the carbonic anhydrase of the brain; it is noteworthy that the formation of cerebrospinal fluid decreases under the influence of the drug.

In some cases acetazolamide improves the condition of patients with pulmonary emphysema as a result of the lowering of the CO₂ pressure in the blood.

Acetazolamide is administered orally. The single dose is 0.25 g (less often 0.5 g). As a diuretic it is taken once a day every day or each second day in courses of 2—4 days with intervals of several days. When administered frequently the diuretic effect decreases since the contents of bicarbonate in the blood fall sharply during the indicated period of time; the bicarbonate contents again rise and the administration of acetazolamide again causes increased excretion of sodium and bicarbonate ions in the urine along with diuresis. Higher doses also do not increase the effect.

Acetazolamide can be combined advantageously with mercury diuretics since it causes acidosis while the latter causes alkalosis; it should also be remembered that when mercury diuretics are administered the sodium ion is excreted together with the chlorine ion, whereas when acetazolamide is administered the sodium ion is for the most part excreted in the form of bicarbonate.

In some cases a diuretic effect begins to appear in patients resistant to mercury diuretics after the administration of acetazolamide. By giving acetazolamide it is possible considerably to reduce the amount of mercury diuretic administered.

A very pronounced diuretic effect is observed when acetazolamide is used in conjunction with aminophylline.

Acetazolamide should not be combined with ammonium chloride or other acid-forming diuretics since in this case the diuretic effect diminishes or even disappears completely.

In glaucoma acetazolamide is prescribed in doses of 0.125—0.25 g 1—3 times a day. Every 5 days a 2-day break is made in treatment. In some cases a good effect is observed when acetazolamide and miotics are administered simultaneously.

In preparation for operations in glaucoma 0.5 g is administered the day before the operation as well as 0.5 g in the morning on the day of the operation

In epilepsy 0.25–0.5 g daily is usually prescribed

Acetazolamide is only slightly toxic and is usually tolerated well by patients even when used over lengthy periods nevertheless in some patients insomnia may appear along with disorientation and paresthesia these symptoms may possibly be associated with inhibition of the carbonic anhydrase of the central nervous system and with hypokalemia When the dose is lowered or the drug withdrawn side effects quickly pass away

When acetazolamide is administered over lengthy periods sodium bicarbonate should be given to preserve the electrolyte balance

Acetazolamide is contraindicated if there is a predisposition to acidosis as well as in patients with a heightened excretion of sodium and potassium ions in Addison's disease and in acute inflammatory diseases of the liver and kidneys

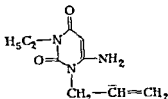
Available in powder form and in tablets of 0.25 g

To be kept in well closed containers observing safety precautions (List B)

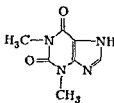
III PYRIMIDINE DERIVATIVES

ALLACIL (Allacilum)

1 Allyl 3 ethyl 6 aminouracil



Allacil



Theophylline

Synonyms Aminometradine Aminometramide Katapyrine Mictine

White crystalline powder sparingly soluble in water (1:50) Melting point 143–144°

Allacil is one of a new group of diuretics that are derivatives of pyrimidine dione or aminouracil. In mode of action and to some extent in chemical structure it is similar to the methylated xanthines for example theophylline. Allacil inhibits the tubular reabsorption of Na and Cl ions the reabsorption of Na is especially strongly depressed — that of Cl is depressed to a less degree there is no change in the excretion of potassium. The blood supply to the kidneys and tuftular filtration are not changed under the influence of allacil the drug also has no effect on the activity of the carbonic anhydrase and the succinic dehydrogenase of the kidneys.

Unlike the mercury diuretics and acetazolamide allacil causes no change in the pH of the urine and in the acid alkali equilibrium.

Allacil is effective when taken orally it has a marked diuretic effect and diminishes congestive manifestations.

Used as a diuretic in patients with cardiovascular insufficiency and in cirrhosis of the liver for the most part in diseases of moderate severity. Allacil is usually inadequate in cardiovascular insufficiency in the stage of acute decompensation and in severe cirrhosis of the liver.

Doses of allacil are individualized depending on the severity of the disease, the effectiveness of the drug and the tolerance shown for it.

The drug is prescribed orally in mild and moderately severe diseases the dose is 0.2–0.8 g (1–4 tablets) a day. It can be taken in cycles of 3–4 days at 4 day intervals or each second day. In cases of pronounced edema the dose can

be increased to 1.2—1.6 g daily during the first few days of treatment. The drug is taken during meals.

Allacil can be prescribed for both in patients and out patients, but careful watch must be kept on patients' general condition and on uretic.

Dyspeptic symptoms may be observed when allacil is used: nausea, vomiting, loss of appetite and diarrhea. Side effects quickly pass away when the drug is withdrawn.

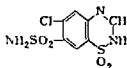
Available in powder form and in tablets of 0.2 g.

To be kept in closed bottles in a place protected from light, observing safety precautions (List B).

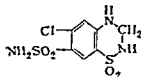
IV. CHLOROTHIAZIDE AND ITS ANALOGUES

CHLOROTHIAZIDE.

6-Chloro-7-sulfamyl-1,2,4-benzothiadiazine 1,1-dioxide



Chlorothiazide



Dihydrochlorothiazide

Synonyms of chlorothiazide: Chlortride, Chlorurit, Diuril, Salurit, Saluric.

White crystalline substance sparingly soluble in water, freely soluble in dilute alkalis.

In chemical structure chlorothiazide resembles acetazolamide and contains a sulfamide group, but in the character of its action it is essentially different from acetazolamide and other inhibitors of carbonic anhydrase. Chlorothiazide may be said to occupy an intermediate position between acetazolamide and the mercurio-organic diuretics. It causes a marked increase in the excretion of Na and Cl ions and to a lesser degree in the excretion of K and bicarbonate ions. It is considered an extremely potent "saluretic".

Since Na and Cl are excreted in equivalent amounts the body's electrolytic balance is not disturbed.

An important feature of chlorothiazide is its effectiveness both in acidosis and alkalosis.

The drug is effective when administered orally and the effect does not decline on lengthy use.

The mode of action of chlorothiazide is not sufficiently clear. It inhibits carbonic anhydrase but in this respect its potency is only about one twentieth that of acetazolamide. The inhibition of the reabsorption of Na and Cl ions which is outwardly similar to that caused by mercury diuretics, also has a different mode of action.

Chlorothiazide is distinguished by its extremely low toxicity, and it can be used for lengthy periods without side effects. It causes no affections of the kidneys.

Chlorothiazide's slight toxicity and its high diuretic potency permit wide application in medical practice.

Indications for the use of chlorothiazide: cardiovascular insufficiency with congestive symptoms in the greater and lesser circulation; cirrhosis of the liver with symptoms of portal hypertension, nephrosis and nephritis (with the exception of severe progressive forms with retarded tubular filtration), toxicosis of pregnancy (nephropathy, edema, eclampsia), edema caused by the use of corticoid hormones, ACTH, etc.

The diuretic effect usually develops within the first two hours after taking chlorothiazide and persists 6—12 hours after a single dose

In addition to the diuretic effect chlorothiazide also has a hypotensive effect. The administration of chlorothiazide to patients with hypertension and without marked edema does not cause any substantial increase in uresis or reduction in body weight but it does have a hypotensive effect. It is possible that this effect is partially associated with the increased excretion of salts; the assumption has also been advanced (Bayer) that by altering the distribution of Na and K in the region of the cellular membranes of the muscles of the blood vessels chlorothiazide causes a lowering of the tone of the arterioles. The use of chlorothiazide in conjunction with ganglion blocking drugs and reserpine considerably intensifies their hypotensive effect. The hypotensive effect of chlorothiazide is intensified when a saltless diet is prescribed at the same time; the drug's ability sharply to increase the excretion of Na and Cl makes it unnecessary strictly to limit patient's consumption of sodium chloride when this is not tolerated well.

Chlorothiazide is prescribed orally in tablets of 0.5 g. The dose is individualized depending on the severity of the disease and the effectiveness of the drug. In light cases 0.5 g is prescribed once or twice a day. In cases of moderate severity 0.5 g is prescribed 2—3 times a day and in severe cases 0.5 g 3—4 times a day or 1 g (2 tablets) twice a day. Increasing the dose above 2 g a day does not cause side effects but there is also no further increase in uresis.

The length of administration depends on the severity of the disease. The drug can be given for 3—5 days in succession followed by a break of 3—4 days after which administration can be resumed. In lighter cases chlorothiazide is taken for 1—2 days with subsequent intervals.

In toxemia of pregnancy chlorothiazide is usually prescribed in a dose of 1 g daily. The frequency of administration must be especially strictly individualized and may vary from once in four days to every day. In severe cases chlorothiazide can be prescribed in a dose of 2 g daily for a short period.

The use of chlorothiazide in conjunction with ganglion blocking substances should likewise be individualized. Doses can range from 0.25 g once a day to 0.5 g 3 times a day depending on the hypotensive effect and the patient's condition. In severe cases of hypertensive disease increasing the dosage of chlorothiazide to 2 g a day is permissible.

Side effects are rarely encountered during treatment with chlorothiazide.

Lengthy intensive use of chlorothiazide may cause hypokalemia and hypochloremic alkalosis. Hypokalemia is observed most often when treating patients with cirrhosis of the liver. Hypokalemia is less pronounced when chlorothiazide is used than is the case with acetazolamide but in individual cases particularly when treating simultaneously with Foxglove preparations the lowering of the potassium content in the blood may predispose patients to the development of arrhythmia.

Hypochloremic alkalosis may develop in cases when intensive chlorothiazide therapy is accompanied by a saltless diet and the loss of chlorides through emesis. In such cases potassium and sodium chloride must be prescribed orally.

In rare cases when large doses are given weakness and dyspeptic upsets may be observed (nausea, vomiting and diarrhea). A short break in treatment is sufficient for overcoming side effects.

When used in conjunction with ganglion blocking drugs chlorothiazide may intensify postural hypotension.

Lately Dihydrochlorothiazide (6-chloro-7-sulfamyl-1,3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide) has also begun to be used as a diuretic. Synonyms: Dihydrochloruril, Disalunil, Esidrex, Esidrix, Hydrochlorothiazide, Hydrodiuril, Hydrosaluric, Hypothiazid, Urodiazin.

In chemical structure dihydrochlorothiazide differs from chlorothiazide only in the absence of a double bond at positions 3,4 of the thiadiazine nucleus (see formula on p. 186); in its action dihydrochlorothiazide is distinguished by being

effective in much smaller doses. The single dose is 0.025—0.05 g and the daily dose — 0.1—0.2 g.

Dihydrochlorothiazide is more readily absorbed from the gastrointestinal tract than chlorothiazide. It is excreted to a greater extent by the kidneys and has a longer diuretic effect (up to 10—12 hours). It causes a somewhat more intensive excretion of chloride ions. The excretion of bicarbonates remains practically unchanged due to the fact that dihydrochlorothiazide has less influence than chlorothiazide on the activity of carbonic anhydrase. There is usually no increase in the excretion of potassium ions.

In optimal doses dihydrochloride approaches the mercury diuretics in the intensity of the diuretic effect.

Like chlorothiazide, dihydrochlorothiazide has a hypotensive action.

Indications for the use of dihydrochlorothiazide are the same as for chlorothiazide.

V ACID-FORMING DIURETICS

AMMONIUM CHLORIDE (Ammonium chloratum) Sal ammoniac NH_4Cl

Synonyms Amchlor Acidamon

White crystalline powder, slightly hygroscopic, odourless, "cooling" saline taste, sublimes on heating, freely soluble in cold water (1:3), more soluble in hot (1:13), sparingly soluble in alcohol.

Ammonium chloride is readily absorbed from the gastrointestinal tract; it is converted into urea in the liver (NH_3) and the chloride ions which are formed react with the bicarbonates of the blood, removing sodium. The excess chlorine is excreted by the kidneys along with the sodium. Reducing the proportion of blood carbonates to carbonic acid leads to the development of acidosis. The sodium retained in the interstitial fluid is drawn on to compensate acidosis and is excreted by the kidneys; a corresponding amount of water is excreted at the same time.

On repeated administration the diuretic effect from ammonium chloride gradually declines. In 21—48 hours the excretion of sodium resulting from the body's compensatory reactions begins to diminish and in 5—7 days the diuretic effect comes to an end; further administration of the drug has no diuretic effect.

Ammonium chloride is chiefly used in edema of cardiac origin; it is often employed to heighten the effect of mercusol and other mercury diuretics.

Ammonium chloride is administered orally; the daily dose for adults is 8—12 g given in several divided doses. It is taken in the form of a 2.5—5% aqueous solution or as a powder in capsules or wafers. The course of treatment is for 5—6 days; if necessary the course of treatment is repeated after a break of several days.

Ammonium chloride should not be prescribed in acute renal affections because of the possibility of uncompensated acidosis.

Ammonium chloride is also effective as an expectorant and is used in bronchitis, pneumonia, etc. Adults are prescribed 0.2—0.5 g 3—5 times a day; children are prescribed doses of 0.1—0.25 g. Administered as a powder in capsules or wafers or in the form of a 0.5—2.5% solution.

Irritation of the stomach, nausea and vomiting may be observed after the administration of ammonium chloride. The drug should be taken after meals in order to lessen dyspeptic symptoms.

Available in powder form. To be kept in well closed bottles in a dry place.

VI PLANT EXTRACTS AND INFUSIONS USED AS DIURETICS

JUNIPER FRUIT, Juniper berries (Fructus Juniperi, Baccae Juniperi)

Dried ripe fruit (cones) of the common Juniper (*Juniperus communis* L.) of the Cypress family (Cupressaceae), commonly called Juniper Berries.

Contain volatile oil (at least 0.5%), sugar, organic acids, resins and other substances

Used as a diuretic, often in conjunction with potassium acetate. Contraindicated in nephritis and nephrosonephritis since they cause inflammation of the renal parenchyma

BEARBERRY LEAF (Folia Uvae ursi)

Leaves of the Bearberry (*Arctostaphylos uva ursi* (L.) Spr.) a perennial bush of the Heath family (*Ericaceae*). Grows in the northern and central European parts of the USSR, and in the Caucasus and Siberia. The leaves contain the glycoside arbutin (15–35%) which undergoes cleavage in the body with the formation of hydroquinone, also contain organic acids, tannin (30–35%) and other substances

Used orally in the form of an infusion or decoction as a diuretic and antiseptic in inflammatory diseases of the bladder and urinary tract. The antiseptic effect is mainly ascribed to the hydroquinone which is excreted with the urine. Bearberry Leaf is an ingredient of diuretic tea

HORSETAIL HERB (Herba Equiseti)

Dried above ground vegetative parts of the Field Horsetail (*Equisetum arvense* L.), family *Equisetaceae*, widely distributed in the Ukraine, the Caucasus, Siberia and Central Asia

Contains a large amount of silica, tannin, saponin, malic acid, mineral salts and other substances

Decoctions and fluid extracts are used as diuretics in cardiac and other diseases accompanied by congestive symptoms

Causes irritation of the kidneys, contraindicated in nephritis and nephrosonephritis

BIRCH BUDS (Betulae gemmae)

Contain volatile oil, resin, saponins, an organic acid (betuloresinic acid) and other substances

Used as a diuretic and cholagogue. When administered orally the possibility of irritation of the kidneys by the resinous substances contained must be borne in mind

BIRCH LEAF (Folia Betulae) is used as a diuretic, does not cause renal irritation

An infusion of Birch Leaf is prepared by pouring boiling water over the chopped leaves. After cooling, sodium bicarbonate is added to dissolve the betuloresinic acid, the infusion is allowed to stand 6 hours, strained and drunk in two portions, the second dose 4 hours after the first

CORNFLOWER FLOWERS (Flores Centaureae cyan L.), family *Compositae*

Used as a mild diuretic in the form of an infusion or tea (a teaspoonful of chopped flowers is steeped in a glass of boiling water, let stand 20 min, cooled and strained). Dose $\frac{1}{4}$ glass 3 times a day 20 min before meals. An ingredient of Diuretic Tea

BURDOCK ROOT (Radix Bardanae) Dried root of the Great Burdock (*Arctium tomentosum* Schr., *Lappa tomentosum* Lam.), family *Compositae*

Used in folk medicine in the form of a decoction as a diuretic and sudorific, also used in gout and rheumatism

Chapter VI

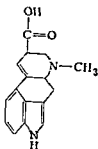
AGENTS WHICH STIMULATE THE UTERINE MUSCLES

I ERGOT AND THE ERGOT ALKALOIDS

ERGOT, SPURRED RYE (*Secale cornutum*)

Ergot is the sclerotium of the fungus *Claviceps purpurea* in the resting stage parasitic on the ovaries of certain cereals principally rye (*Secale cereale*). Oblong sclerotia almost triangular in section with three longitudinal grooves somewhat curved at both ends 1—3 cm long and up to 3—5 mm thick externally violet black dull. Contain alkaloids histamine tyramine choline acetylcholine and other substances.

Ergot contains at least 0.05% alkaloids. The principal alkaloids are ergotamine ergotamine and ergometrine (see also Adrenolytic agents p 114). The basic unit in the chemical structure of the ergot alkaloids is lysergic acid a derivative of indole. Ergotamine and the alkaloids of the ergotamine group are insoluble in water they are complex peptid derivatives of lysergic acid. Ergometrine is a water soluble alkaloid it has a simpler structure being the β propanolamide of lysergic acid.



Lysergic acid

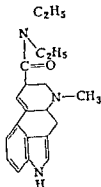
The ergot alkaloids have a complicated influence on the body. They cause contraction of the smooth muscles. ergotamine and the alkaloids of the ergotamine group especially their hydrogenated derivatives have an adrenolytic effect. One of the characteristic pharmacological properties of the ergot alkaloids is their power of intensifying and accelerating rhythmic uterine contractions.

and raising the tone of the uterus this is especially marked in ergometrine and ergotamine. The uterine muscles are particularly sensitive to ergot during pregnancy and after childbirth.

The ergot alkaloids also have a complicated influence on the central nervous system. Ergotamine and ergotamine as well as their hydrogenated derivatives have a sedative effect, lower basic metabolism and lessen tachycardia (in exophthalmic goiter, hypersympathicotonia, etc.). Ergotamine often has a good effect in migraine; it aborts or prevents attacks.

Some synthetic derivatives of lysergic acid which are similar in structure to the ergot alkaloids have a strong influence on the central nervous system.

Lysergic acid diethylamide (LSD₂₅, Delysid, Lysergide) is one of the most potent "hallucinogenic" substances. In very small doses (1 mg per kg of body weight) it causes a temporary impairment of higher nervous activity with the development of visual and auditory hallucinations, unrest, etc.



Lysergic acid-d diethylamide

According to modern conceptions, this effect of lysergic acid diethylamide is associated with its influence on the metabolism of serotonin (5-hydroxytryptamine, see p. 32) to which it is similar in chemical structure and of which it is the pharmacological antagonist.

The ergot alkaloids and their derivatives are used as substances which have an influence on various bodily functions. Dihydroergotamine and dihydroergotamine are employed in vascular spasm and in hypertensive and other diseases. A mixture of ergotamine tartrate (1 mg) and caffeine (0.1 g) is put out in the USSR under the name of *Coffetamine* (*Coffetaminum*). It is taken for migraine and headache of diverse etiology in doses of 1–2 tablets (dragees) up to 4 tablets a day. *Coffecristine* (*Coffecristinum*, synonym — *Secadol*) has been proposed for the same purpose; it contains 0.5 mg ergocryptine ethanesulfonate and 0.1 g caffeine. It is also taken in doses of 1–2 tablets up to 4 tablets a day.

Ergotamine and ergotamine are used in conjunction with barbiturates and Belladonna preparations in autonomic dystonia, neuroses and hyperthyroidism.

Lysergic acid diethylamide finds application for the most part in experimental investigations; it is sometimes used in psychiatric practice.

Ergot preparations have long enjoyed wide application in obstetrics and gynecology in atony of the uterus and associated uterine hemorrhage. The hemostatic effect is chiefly due to the compression of the walls of the vessels during contraction of the uterine muscles.

The use of ergot preparations is contraindicated during pregnancy and labor (tonic contraction of the uterine muscles may cause asphyxia of the foetus).

The following ergot preparations are used as uterine agents:

Ergot Powder (*Pulvis Secalis cornuti*) (*List B*)

Violet grey powder obtained from Ergot which has been freed of fatty oil

Synonym Styphcin

Yellow fine crystalline powder, odourless bitter taste, hygroscopic very freely soluble in water (1:1) freely soluble in alcohol (1:2) Solutions are sterilized by holding at 100° for 30 min

Has a tonic influence on the musculature of the internal organs especially the uterus

Prescribed in uterine hemorrhage associated with fibroma and inflammatory processes in a dosage of 0.05 g orally 3 times a day, or 1 ml 2–5% solution subcutaneously

Maximal doses for adults single — 0.1 g, daily — 0.3 g

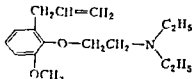
Used topically in the form of a 1–2% solution to arrest hemorrhage

Available in powder form and in tablets (dragees) of 0.05 g

To be stored in well closed bottles of amber glass in a place protected from light observing safety precautions (List B)

PREGNANTOL (Pregnantolum)

2-Methoxy-6-allylphenol diethylaminoethyl ether



Synonym Gravitol

Causes constriction of the vessels and contraction of the muscles of the uterus. Has a weak adrenolytic effect. Judging by experimental findings the action on the uterus is not constant in some experiments pregnantol causes relaxation of the muscles (F. G. Kyaer Kingisepp)

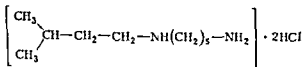
Used in atony and hypotonia of the uterus during labour and in insufficient contraction of the uterus during the puerperium as well as in uterine hemorrhage associated with inflammatory processes

Prescribed orally subcutaneously and intramuscularly. Orally 1 tablet (0.02 g) is administered 3–4 times a day after meals subcutaneously and intramuscularly 1 ml 1% solution is injected 1–2 times a day

Available in tablets of 0.02 g in the form of the citrate, and in ampoules containing 1 ml 1% solution of the hydrochloride

ISOVERINE (isoverinum)

N-Isoamylcadaverine dihydrochloride



White crystalline powder freely soluble in water. Melting point 293–295°. Aqueous solutions are sterilized by holding at 100° for 30 min

Isoverine is similar in pharmacological properties to Sphaerophysine (p. 113) it also blocks the ganglia of the autonomic division of the nervous system lowers arterial pressure, raises the tone and intensifies the contractions of the uterine muscles and heightens the sensitivity of the uterus to pituitary extract

Used as an agent to accelerate labour (better in conjunction with pituitary extract or other labour accelerating drugs) and to hasten the contraction of the uterine musculature during the puerperium. Because of its hypotensive effect isoverine can be prescribed for parturient women who are suffering from late toxemia of pregnancy accompanied by hypertension

Administered intramuscularly in a dose of 1 ml 2 or 5% solution Can likewise be given by mouth in dose of 0.1 g (2—3 times), when administered intramuscularly the effect is more constant

Available in ampoules containing 1 ml 2% and 5% solution, and in tablets of 0.1 g

To be stored under ordinary conditions

EUROPEAN BARBERRY (*Berberis vulgaris* L.)

Bush of the Barberry family (*Berberidaceae*) Habitat European part of the USSR

Contains alkaloids, including berberine, oxyacanthine, berbamine, leontidine etc

A 20% infusion made with 40° alcohol is used for medicinal purposes Transparent dark yellow liquid of slightly acid taste and characteristic odour

Causes contraction of the smooth muscles of the uterus and constriction of the vessels, somewhat heightens the coagulability of the blood Has a moderate choleric effect

The plant's pharmacological properties are mainly due to the berberine it contains

Used in obstetrics and gynecology in atonic hemorrhage during the puerperium and in subinvolution of the uterus, as well as in hemorrhage associated with inflammatory processes

Administered orally, 30—40 drops 2—3 times a day Period of treatment 2—3 weeks

To be stored in a cool place protected from light, observing safety precautions

AMUR BARBERRY (*Berberis amurensis*)

Effect and indications for use the same as for European Barberry Used in the form of an infusion made with 40° alcohol 25—30 drops 3 times a day

To be stored in a cool place protected from light, observing safety precautions

SHEPHERD'S PURSE HERB (*Herba Bursae pastoris*)

Shepherd's Purse (*Capsella bursa pastoris* L. Medie) family *Cruciferae*, found everywhere in the USSR contains choline, acetylcholine tyramine, organic acids, saponins and other substances The dried above ground parts with leaves, flowers and fruit are used Has the power of causing contraction of the uterine muscles

Used in the form of infusions and fluid extract in atony of the uterus and in uterine hemorrhage

Fluid Extract of Shepherd's Purse (*Extractum Bursae pastoris fluidum*) 10% extract prepared with 70° alcohol Transparent greenish brown liquid with characteristic odour and pungent taste

Administered orally in doses of 20—25 drops 2—3 times a day

BETONY (*Stachys betonicaeflora*)

Herb of the Mint family (*Labiatae*), habitat — Kirghiz SSR An alcoholic infusion is used, dark green liquid of pleasant taste

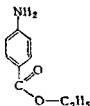
Prescribed during the puerperium in subinvolution of the uterus and in hemorrhage associated for the most part with inflammatory processes 1 teaspoonful diluted with 3 spoonfuls of boiling water is given 2—3 times a day

Chapter VII

AGENTS ACTING PREEMINENTLY IN THE REGION OF THE SENSORY NERVE ENDINGS

I. LOCAL ANESTHETICS

ETHYL AMINOBENZOATE (*Aethylus aminobenzoas*).
Ethyl ester of *p* aminobenzoic acid



Synonyms *Anaesthalgin, Anaesthacin, Anaesthesin, Anaesthin, Anestezyna, Anesthone, Benzocain, Ethoforme, Norcainum, Parathesin, Rhaetocaline, Top analgin*.

White crystalline powder, odourless, slightly bitter taste, causes transitory numbness of tongue, very slightly soluble in cold water, more soluble in boiling water, soluble in 5 parts of alcohol, freely soluble in fats, fatty oils, ether and chloroform. Melting point $80-91.5^\circ$.

Has a local anesthetic effect. Not used as an anesthetic in operations because of its low solubility in water. Used in the form of 5–10% ointment or dusting powder in urticaria and skin diseases accompanied by itching, and also for analgesia of wound and ulcerous surfaces. In diseases of the rectum (fissures, pruritus, hemorrhoid) suppositories containing 0.05–0.1 g of the drug are used. For anesthesia of the mucous membranes, 5–20% oil solutions are used. Prescribed orally in powders and mucilaginous mixtures for analgesia of the mucous membranes in gastric neuroses, heightened sensitivity of the oesophagus, etc. Sometimes prescribed in cyclic vomiting, vomiting of pregnancy, seasickness and airsickness. Dosage for adults 0.25–0.3 g 3–4 times a day. Dosage for children up to 1 year old — 0.02–0.04 g, from 2 to 5 years — 0.05–0.1 g, from 6 to 12 years — 0.12–0.25 g.

Maximal doses for adults single — 0.5 g, daily — 1.5 g

Maximal doses for children up to 6 months old, single — 0.025 g, daily — 0.075 g, from 6 months to 1 year, single — 0.04 g, daily — 0.12 g, 2 years, single — 0.06 g, daily — 0.18 g, 3—4 years, single — 0.08 g, daily — 0.24 g, 5—6 years, single — 0.12 g, daily — 0.36 g, 7—9 years, single — 0.16 g, daily — 0.5 g, 10—14 years, single — 0.2 g, daily — 0.6 g

Available in powder form

To be kept in well closed bottles in a place protected from light, observing safety precautions (List B)

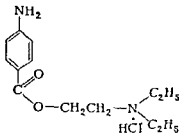
Ethyl aminobenzoate suppositories Composition ethyl aminobenzoate 0.05 g, extract of Polygonum hydropiper 0.06 g, zinc oxide 0.016 g, activated charcoal 0.01 g, fatty base 2.2 g

Used for alleviating pain, itching and spasms in hemorrhoid Introduced into the rectum, 1—2 suppositories a day

Suppositories of the following composition are also available ethyl amino benzoate 0.1 g, bismuth subgallate 0.04 g, zinc oxide 0.02 g, menthol 0.004 g, base for suppository 2 g

PROCAINE HYDROCHLORIDE (Procaini hydrochloridum)

Hydrochloride of the diethylaminoethyl ester of p aminobenzoic acid



Synonyms Aethocaine, Allocaine, Alokain, Ambocain, Aminocaine, Anestho-
caine, Aristokain, Atoxicaine, Bernacaine, Cerocain, Chemocain, Citocain,
Dorecain, Ericain, Ethocaine, Frekain, Genocaine, Herocaine, Isocaine, Jena-
cain, Juvocaine, Kerokaine, Marecaine, Minocain, Naucain, Neocaine, Novo-
caine, Panocain, Paracaine, Pharmacaine, Planocaine, Polocainum, Popocain, P,
Protocaine, Resorcaine, Scurocaine, Sevicaine, Syncaine, Syntocain, Thilocain,
Topocain

Colourless crystals, odourless. Melting point 154—156°. Very freely soluble
in water (1 : 1), freely soluble in alcohol (1 : 8). Aqueous solutions are sterilized
by holding at 100° for 30 min. Solutions of procaine hydrochloride are easily
hydrolyzed if alkaline, they are stabilized by addition of 0.1 N hydrochloric
acid at the rate of 3 ml per liter for 0.25% solution, 4 ml for 0.5% solution and
9 ml for 1% and 2% solution. pH of solution = 3.8—4.5.

Procaine hydrochloride acts as a local anesthetic, it is less potent than
cocaine but considerably less toxic and has a much broader range of therapeutic
action.

Procaine hydrochloride is widely used for infiltration and spinal anesthesia,
it is little suited for surface anesthesia since it slowly penetrates through the
intact mucous membranes.

When absorbed or introduced directly into the blood stream, procaine hydro-
chloride has a general influence on the body: it lessens the formation of acetyl-
choline and lowers the excitability of the peripheral cholinoreactive systems,
has a blocking effect on the autonomic ganglia, abates spasms of the smooth
muscles, and lowers the excitability of the myocardium and the motor zones of
the cerebral cortex. In toxic doses it causes stimulation of the central nervous
system followed by paralysis.

Procaine hydrochloride is quite rapidly hydrolyzed in the body with the formation of para aminobenzoic acid and diethylaminoethanol¹

To diminish the absorption of procaine hydrochloride solutions during local anesthesia and prolong their action 0.1% adrenalin hydrochloride is usually added at the rate of 1 drop per 2.5 or 10 ml of procaine hydrochloride. The addition of adrenalin is particularly necessary owing to the fact that procaine, unlike cocaine, does not cause constriction of the vessels.

The concentration and amount of procaine hydrochloride solution used depend on the character of operative intervention, method of application, the patient's condition and age, etc. Something that must be taken into account is that for the same total dose of the drug, the toxicity is higher when more concentrated solutions are used.

For infiltration anesthesia a 0.25–0.5% solution is used for A. V. Vishnevsky's method of anesthesia (light creeping infiltration) — 0.125–0.25% solution for conduction anesthesia — 1–2% solution for peridural anesthesia — 2% solution (20–25 ml) for spinal anesthesia — 5% solution (2–3 ml). Solutions for peridural and spinal anesthesia are prepared with twice distilled water. Procaine chloride is also used for intraosseal anesthesia.

Procaine hydrochloride is sometimes used in otorhinolaryngological practice for anesthesia of the mucous membranes. A 10–20% solution is necessary in order to obtain a superficial anesthetic effect.

Procaine hydrochloride is being widely used today for the treatment of various diseases. The so called "procaine block" is for the purpose of weakening interoreceptive reflex reactions involved in the development of the pathological process.

For paranephric block (A. V. Vishnevsky's method) 50–80 ml 0.5% solution or 100–150 ml 0.25% procaine hydrochloride is injected into the paranephric tissue.² For vago sympathetic block 30–100 ml of 0.25% solution is injected.

Procaine hydrochloride solutions are also administered intravenously and orally in hypertensive disease, late toxicosis of pregnancy with a hypertensive syndrome, spasms of the blood vessels, phantom limb syndrome, ulcer of the stomach and duodenum, pruritus, neurodermatitis, eczema, keratitis, iridocyclitis, glaucoma, etc. Intravenously, from 1 to 10 or 15 ml of 0.25–0.5% solution is prescribed. The injection must be made very slowly — preferably in isotonic saline. The number of injections (sometimes up to 10 or 20) depends on the severity of the disease and the effectiveness of treatment.

Orally 30–50 ml 0.25–0.5% solution is administered 2–3 times a day.

Intradermal injections of 0.25–0.5% solution are used for circular and paravertebral block in eczema, neurodermatitis, sciatika, etc.

Since procaine hydrochloride has the power of diminishing the excitability of the myocardium, it is sometimes prescribed in fluttering arrhythmia. 2–5 ml of 0.25% solution is administered intravenously up to 4–5 times (see Procaine amide p. 161).

Procaine hydrochloride is also used for dissolving penicillin in order to prolong its action (see Penicillin).

Procaine hydrochloride has also been proposed for use in the form of intramuscular injections in certain diseases which more often occur in advanced age — endarteritis, atherosclerosis, hypertensive disease, spasms of the coronary and cerebral vessels, bronchial asthma, diseases of the joints of rheu-

¹ The cleavage products of procaine are pharmacologically active substances. Para aminobenzoic acid (vitamin H) is an integral part of folic acid. In the bound state it is also a constituent of other compounds found in vegetable and animal tissues. Para aminobenzoic acid is a growth factor for bacteria. In chemical structure it is similar to the sulfanilamide drugs acting concurrently with the latter, para aminobenzoic acid inhibits their antibacterial effect (see Sulfanilamide drugs). Procaine, being a derivative of para aminobenzoic acid, also has a pronounced anti sulfanilamide action. Diethylaminoethanol has a moderate vasodilator effect.

² The paranephric block must be performed with care, on an inpatient basis.

matic and infectious etiology etc Treatment is carried out on an inpatient basis 5 ml of 2% procaine hydrochloride solution is injected intramuscularly 3 times a week the course consists of 12 injections after which a 10 day break is made During the year up to 4 courses of treatment can be given A favourable effect is chiefly observed in the early stages of diseases associated with functional impairment of the nervous system

Whatever the method of administration procaine hydrochloride must be used with caution In some patients a heightened sensitivity to procaine is observed (vertigo general weakness fall of the arterial pressure collapse shock) Skin reactions may develop dermatitis peeling etc Procaine hydrochloride is at first prescribed in small doses in order to reveal heightened sensitivity When administering procaine hydrochloride intramuscularly 2 ml of 2% solution is first prescribed if there are no side effects 3 ml of the same solution is administered in 3 days and only then administration of the full dose — 5 ml per injection — is begun

Maximal doses for adults single orally — 0.25 g intramuscularly (2% solution) — 0.1 g, intravenously (0.25% solution) — 0.05 g daily orally — 0.75 g intramuscularly and intravenously — 0.1 g

The following maximal doses have been established for infiltration anesthesia (for adults) first single dose at beginning of operation — not more than 1.25 g when using 0.25% solution (i.e., 500 ml of solution) and 0.75 g when using 0.5% solution (150 ml of solution) Subsequently during each hour of the operation — not more than 2.5 g when using 0.25% solution (1000 ml of solution) and 2 g when using 0.5% solution (400 ml of solution)

Available in powder form and in ampoules containing 1 ml 1% solution 2 ml 0.5% 1% and 2% solution 5 ml 0.5% and 2% solution 10 ml 0.5% and 1% solution

To be kept in well stoppered bottles or sealed ampoules in a place protected from light observing safety precautions (List B)

Oil solution of procaine base (Solutio Procaini oleosa) Solution of procaine base in persic oil Sterile transparent liquid of light yellow colour Available in ampoules containing 5 ml 5% solution

Unlike the chloride procaine base is insoluble in water when oil solutions are injected into the subcutaneous tissue or the muscles they are slowly absorbed and have a prolonged local anesthetic effect The preparation must not be injected into the blood vessels because of the danger of fat embolism

Anesthesia usually sets in within 1—3 hours after administration The duration of the effect from a single injection ranges from 3 to 15 days

Indication for use marked protracted pain in cases of limited pathological processes (painful cicatrices fissures of the anus a pathological process following operation for hemorrhoid etc.) A single injection of 5—10 ml of the preparation is given The injection is performed with a syringe connected to a thick needle The ampoule is warmed to body temperature before use. The needle is first sunk to the necessary depth and when it is certain that it has not entered a blood vessel the syringe is attached and the necessary amount of the preparation is slowly injected into the area of the pain focus and the surrounding tissues gradually moving the needle to the surface of the skin Without drawing the needle out completely the point is moved in different direction under the skin and the rest of the solution injected where necessary Before administering the drug it is advisable to anesthetize the skin at the site of the injection with a 0.25—0.5% aqueous solution of the usual procaine hydrochloride Contraindications to the use of the preparation 1) when there is danger of the needle entering a blood vessel 2) in suppurative processes 3) when the skin is inflamed at the site of injection

The solution is to be stored in sealed ampoules in a cool place protected from light

Procaine hydrochloride is quite rapidly hydrolyzed in the body with the formation of para aminobenzoic acid and diethylaminoethanol¹

To diminish the absorption of procaine hydrochloride solutions during local anesthesia and prolong their action 0.1% adrenalin hydrochloride is usually added at the rate of 1 drop per 2.5 or 10 ml of procaine hydrochloride. The addition of adrenalin is particularly necessary owing to the fact that procaine unlike cocaine does not cause constriction of the vessels.

The concentration and amount of procaine hydrochloride solution used depend on the character of operative intervention, method of application, the patient's condition and age etc. Something that must be taken into account is that for the same total dose of the drug the toxicity is higher when more concentrated solutions are used.

For infiltration anesthesia a 0.25–0.5% solution is used for A. V. Vishnevsky's method of anesthesia (tight creeping infiltration) — 0.125–0.25% solution for conduction anesthesia — 1–2% solution for peridural anesthesia — 2% solution (20–25 ml) for spinal anesthesia — 5% solution (2–3 ml). Solutions for peridural and spinal anesthesia are prepared with twice distilled water. Procaine chloride is also used for intraosteal anesthesia.

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Procaine hydrochloride solutions are also administered intravenously and orally in hypertensive disease, late toxicosis of pregnancy with a hypertensive syndrome, spasms of the blood vessels, phantom limb syndrome, ulcer of the stomach and duodenum, pruritus, neurodermatitis, eczema, keratitis, iridocyclitis, glaucoma etc. Intravenously from 1 to 10 or 15 ml of 0.25–0.5% solution is prescribed. The injection must be made very slowly — preferably in isotonic saline. The number of injections (sometimes up to 10 or 20) depends on the severity of the disease and the effectiveness of treatment.

Orally 30–60 ml 0.25–0.5% solution is administered 2–3 times a day. Intradermal injections of 0.25–0.5% solution are used for circular and paravertebral block in eczema, neurodermatitis, sciatica etc.

Since procaine hydrochloride has the power of diminishing the excitability of the myocardium it is sometimes prescribed in fluttering arrhythmia. 2–5 ml of 0.25% solution is administered intravenously up to 4–5 times (see Procaine amide p. 161).

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Maximal doses for adults single orally — 0.25 g intramuscularly (2% solution) — 0.1 g intravenously (0.25% solution) — 0.05 g daily orally — 0.75 g intramuscularly and intravenously — 0.1 g

The following maximal doses have been established for infiltration anesthesia (for adults) first single dose at beginning of operation — not more than 1.25 g when using 0.25% solution (i.e. 500 ml of solution) and 0.75 g when using 0.5% solution (150 ml of solution) Subsequently during each hour of the operation — not more than 2.5 g when using 0.25% solution (1000 ml of solution) and 2 g when using 0.5% solution (400 ml of solution)

Available in powder form and in ampoules containing 1 ml 1% solution 2 ml 0.5% 1% and 2% solution 5 ml 0.5% and 2% solution 10 ml 0.5% and 1% solution

To be kept in well stoppered bottles or sealed ampoules in a place protected from light observing safety precautions (List B)

Oil solution of procaine base (Solutio Procaini oleosa) Solution of procaine base in persic oil Sterile transparent liquid of light yellow colour Available in ampoules containing 5 ml 5% solution

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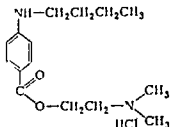
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Indication for use marked protracted pain in cases of limited pathological processes (painful cicatrices fissures of the anus a pathological process following operation for hemorrhoid etc) A single injection of 5—10 ml of the preparation is given The injection is performed with a syringe connected to a thick needle The ampoule is warmed to body temperature before use The needle is first sunk to the necessary depth and when it is certain that it has not entered a blood vessel the syringe is attached and the necessary amount of the preparation is slowly injected into the area of the pain focus and the surrounding tissues gradually moving the needle to the surface of the skin Without drawing the needle out completely the point is moved in different direction under the skin and the rest of the solution injected where necessary Before administering the drug it is advisable to anesthetize the skin at the site of the injection with a 0.25—0.5% aqueous solution of the usual procaine hydrochloride Contraindications to the use of the preparation 1) when there is danger of the needle entering a blood vessel 2) in suppurative processes 3) when the skin is inflamed at the site of injection

The solution is to be stored in sealed ampoules in a cool place protected from light

DICAIN (Dicainum)

Hydrochloride of the dimethylaminoethyl ester of p butylaminobenzoic acid



Synonyms Amethocaine Anelaine Butelhanol Decicaine Felicam Foncaine Intercaim Medicain Pantocaine Panlocaine hydrochloride Rexocaine Tetracaini hydrochloridum

White to slightly yellowish crystalline powder odourless soluble in water (1:10) in alcohol (1:6) insoluble in ether Melting point 147—150°

Solutions are sterilized by holding at 100° for 30 min they are stabilized by the addition of 2 drops of dilute hydrochloric acid per 100 ml of solution

Dicain is a strong local anesthetic considerably more potent than procaine hydrochloride and cocaine At the same time dicain is highly toxic twice as toxic as cocaine and ten times as toxic as procaine hydrochloride For that reason it must be used with caution

At present dicain is used for the following purposes a) In ocular practice when removing foreign bodies and in various operations Dose 2—3 drops of 0.25% 0.5% 1% or 2% solution Pronounced anesthesia develops in 1—2 min. When using dicain in ocular practice it must be borne in mind that solutions of higher concentration than 2% can cause injury to the corneal epithelium as well as considerable dilation of the conjunctival vessels Ordinarily a 0.5% solution is sufficient for anesthesia during surgical operations on the eye In order to intensify and prolong the effect 0.1% adrenalin solution is added (3—5 drops per 10 ml of dicain solution) For anesthesia when measuring the intraocular pressure a 0.1% dicain solution is adequate Dicain is not used in keratitis b) In otorhinolaryngological practice in certain operations (puncture of the antrum of Highmore removal of adenoids conchotomy operations on the middle ear) Since dicain is rapidly absorbed by the mucous membranes of the respiratory passages great caution must be observed when it is used and careful watch must be kept on the patient's condition Children up to 10 years old are not given anesthesia with dicain in older children a maximum of 1—2 ml of 0.5—1% solution is used In adults up to 3 ml of 1% solution is used and only when absolutely necessary 2% or 3% solutions In the absence of contraindications to the use of vasoconstrictor substances adrenalin or ephedrine is added (1 drop of 0.1% adrenalin per 1—2 ml of dicain solution or 1 drop of 2—3% ephedrine per ml of dicain) The dicain is applied to the mucous membrane by means of a tampon moistened with the solution The tampon must not be left long in the nasal cavity Painting or atomizing the pharynx and larynx is performed gradually at intervals while keeping watch on the patient's condition In order to diminish the general reaction to dicain it is advisable to give the patient 0.1 g amobarbital sodium—30—60 min before anesthesia Whenever possible procaine hydrochloride should be used instead of dicain At the first symptoms of dicain intoxication the mucous membranes should be washed with a solution of sodium bicarbonate or with physiological solution and a solution of caffeine sodium benzoate injected subcutaneously other measures should be carried out depending on the picture of the intoxication The use of dicain in the form of drops for the nose is impermissible c) For anesthesia in broncho and oesophagoscopy and bronchography

while observing the precautionary measures mentioned d) *For peridural anesthesia* The use of dicain for this purpose requires particular caution The solution is prepared immediately before the operation with isotonic saline in a concentration of 0.3% (3:1000) 33 ml of sterile physiological solution is boiled 1½–2 min in a flask of neutral glass 0.1 g of dicain powder is then added to the not (not boiling) physiological solution The dicain solution is again brought to boiling (it should not be boiled!) After the dicain has completely dissolved the solution is cooled it is then ready for use

6–7 drops of 0.1% adrenalin solution are added to the dicain solution immediately before anesthesia (1 drop to 5 ml of the anesthetic solution) The solution is not warmed before using For anesthesia 15–20 ml 3:1000 solution is used (for weak and aged patients not more than 15 ml is administered) The injection is carried out in 3 or 4 stages 5 ml is first administered followed by a wait of 5 min to be sure that the solution did not enter the spinal canal the next 5 ml is then administered and this procedure is continued until the necessary amount of dicain has been injected If the first 5 ml enters the spinal canal administration is discontinued Peridural anesthesia with dicain requires great attention the full dose of dicain must not be injected into the spinal canal

Maximal doses for adults for anesthesia of the upper respiratory passages — single administration of 0.09 g (3 ml of 3% solution) for peridural anesthesia — single administration of 0.075 g (25 ml of 0.3% solution)

Doses of dicain must not be exceeded because of the danger of serious toxic manifestations Fatal cases have been described in the literature following overdosage and incorrect use of dicain

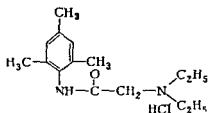
When using dicain instruments and syringes must not contain residues of alkali since dicain is precipitated from alkaline solutions

Available in powder form

To be kept locked (List A) in well stoppered glass bottles

TRIMECAIN (Trimecainum)

Diethylamino 2,4,6-trimethylacetanilide hydrochloride



Synonym Mesocain

White crystalline powder freely soluble in water Melting point 136–137° Solutions are sterilized by holding at 100° for 30 min

Trimecain is a potent local anesthetic it gives deeper and more prolonged conduction and infiltration anesthesia than procaine hydrochloride It does not give sufficiently pronounced terminal anesthesia The toxicity is relatively low

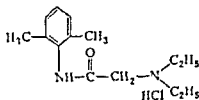
Trimecain (like xycaïn) differs from procaine in not having an antisulf anilamide action since its molecule does not contain a p-aminobenzoic acid residue (see p. 197)

For infiltration anesthesia a 0.25% 0.5% or 1% solution is used up to 800 ml of 0.25% solution is administered up to 400 ml of 0.5% solution and up to 100 ml of 1% solution

For conduction anesthesia up to 100 ml of 1% solution is used or up to 20 ml of 2% solution

A solution of adrenalin hydrochloride can be added to trimecain solutions to intensify and prolong the anesthetic effect (see Procaine Hydrochloride)

Contraindications to the use of trimecain diseases of liver and kidneys
 Safety precautions are to be observed in storage (List B)
XYCAIN (Xycainum)
 Diethylamino 2,6 dimethylacetanilide hydrochloride



Synonyms Astracaine Isicaina Leostesin Lidocaini hydrochloridum, Lidocain Lignocain Maricain Solcain Xylestesin Xylocaine hydrochloride Xylotilin Xyloton Xylotox

White or slightly yellowish crystalline powder bitter taste freely soluble in water soluble in alcohol insoluble in ether hygroscopic Turns yellow on long exposure to light Melting point 128—129° Solutions are prepared with twice distilled water and are sterilized by holding at 100° for 30 min

In chemical structure xycain is closely related to trimecain differs from the latter in having no methyl group in the para position in the benzene nucleus

Xycain is a potent local anesthetic and gives all forms of local anesthesia terminal infiltration and conduction Acts more rapidly than procaine hydrochloride and the effect is stronger and more prolonged Unlike procaine hydrochloride xycain does not diminish the antibacterial action of sulfanilamides The relative toxicity of xycain depends on the concentration of the solution In low concentrations (0.5%) the toxicity does not differ significantly from that of procaine hydrochloride in higher concentrations (1 and 2%) the toxicity increases by 10–50%

Xycain can be used for various forms of local anesthesia in surgery gynecology urology stomatology ophthalmology and otorhinolaryngology

Xycain solutions are compatible with solutions of adrenalin hydrochloride the addition of adrenalin retards absorption and intensifies the effect while lowering toxicity

For infiltration anesthesia 0.25—0.5% solutions are used a 0.5% solution is chiefly employed in minor operations A concentration of 0.25% is used for operations requiring more than 500 ml of solution the total amount of 0.25% solution for the operation should not exceed 1000 ml and the total amount of 0.5% solution — 500 ml For conduction anesthesia 0.5–1 or 2% solutions are used (up to 50 ml) For painting the mucous membranes (for tracheal intubation broncho oesophagoscopy removal of adenoids puncture of the antrum of Highmore etc) a 1—2% solution is used less frequently a 5% solution the volume not to exceed 20 ml

Xycain can likewise be used for peridural and intraosseal anesthesia For conduction and peridural anesthesia 1 drop of 0.1% adrenalin hydrochloride solution is added ex tempore per 10 ml of xycain but not more than 5 drops for the entire amount of solution

Xycain is usually tolerated well the arterial pressure pulse and respiration do not change significantly and there are no symptoms of local irritation

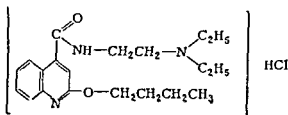
When the drug enters the blood stream rapidly there may be a lowering of the arterial pressure and collapse the hypotensive effect is reduced by the administration of ephedrine

Xycain is contraindicated in cardiovascular insufficiency and impairment of the function of liver and kidneys

To be stored in hermetically sealed containers in a place protected from light, observing safety precautions (List B)

SOVCAIN (Sovcainum)

α Butoxy-(diethylaminoethyl) cinchonamide hydrochloride



Synonyms Butylcaine, Cincaïne, Cinchocaine, Cinchocaini hydrochloridum, Dibucaine, Nupercaine, Nuporal, Optocain, Percaine, Percamine, Quinocaine

White or slightly yellowish crystalline powder, freely soluble in water and alcohol, insoluble in ether

Used as a local anesthetic

Sovcain is 15–20 times more potent than procaine hydrochloride and the effect persists approximately 3 times as long. At the same time it is highly toxic (15–20 times more toxic than procaine hydrochloride and 5 times more toxic than cocaine), and is slowly excreted, for that reason it must be used with great caution.

Sovcain is chiefly used for spinal anesthesia. It is injected into the spinal canal in the form of a 0.5–1% solution. The amount of solution depends on the character of the operation, the patient's age and condition etc. Adults are usually given 0.8–0.9 ml of solution, and children from 8–10 years old—0.3–0.4 ml. Since sovcain often causes a lowering of the arterial pressure patients are first given a subcutaneous injection of 1 ml 5% ephedrine solution (patients with high arterial pressure are not given ephedrine).

Maximum dose for injection into the spinal canal (for adults) single administration of 0.01 g (1 ml 1% solution)

Since sovcain intensifies the effect of procaine hydrochloride, it is sometimes used in small doses mixed with procaine hydrochloride for infiltration anesthesia. When using sovcain instruments and syringes should be free of residues of alkali, since sovcain is precipitated from alkaline solution.

Available in powder form and in ampoules containing 1 ml 0.5% and 1% solution.

To be kept locked (List A) in well stoppered bottles of amber glass

II. EMOLLIENTS AND ADSORBENTS

WHITE CLAY (Bulus alba) Kaolin

Aluminium silicate with small admixture of calcium and magnesium silicates

White powder with yellow or greyish tint, unctuous, insoluble in water and dilute acids, readily forms a plastic mass when mixed with small amount of water. Has emollient and adsorptive properties.

Administered topically in the form of dusting powders, pastes or ointments in skin diseases, ulcers, prickly heat, burns, etc. Administered orally in gastrointestinal diseases (colitis, enteritis etc.) and in cases of poisoning adults are prescribed from 20 or 30 up to 100 g, children—5–10 g. Also used as excipient for pills and tablets containing medicaments which are easily decomposed in the presence of organic substances (silver nitrate, potassium permanganate).

kaolin and other clays intended for medicinal purposes are dispensed after obligatory sterilization in the drying oven for 90 min at a temperature of 160°

Available in powder form

To be kept in well closed bottles

TALC (Talcum)

Magnesium silicate of approximately the following composition

$4 \text{ SiO}_2 \cdot 3 \text{ MgO} \cdot \text{H}_2\text{O}$

Very fine white or slightly greyish powder, odourless and tasteless adheres to skin unctuous almost insoluble in water, acids and other solvents Sterilized in drying oven for 90 min at a temperature of 160° Used for dusting powders as well as an indifferent filler for pastes and tablets

MAGNESIUM TRISILICATE (Magnesium trisilicicum)

$\text{Mg}_2\text{Si}_2\text{O}_5 \cdot (\text{H}_2\text{O})_n$

Synonyms Banacid Magnosil Magsorbent

White amorphous powder, odourless and tasteless insoluble in water, decomposed by mineral acids

Used as adsorbent emollient and antacid in hyperacidity of gastric juice ulcer of the stomach and duodenum and other diseases of the gastrointestinal tract On entering the stomach magnesium trisilicate changes to a jelly like condition reacting with the acid of the gastric juice according to the equation



During this reaction 1 g of magnesium trisilicate neutralizes 155 ml 0.1 N hydrochloric acid Neutralization proceeds slowly, magnesium trisilicate is a slow acting antacid Hydrochloric acid is neutralized without the formation of gases and without subsequent compensatory formation of increased amounts of hydrochloric acid The colloidal mass formed when magnesium trisilicate enters the stomach has a high adsorptive capacity it also protects the mucous membrane of the stomach from the action of pepsin and hydrochloric acid The magnesium chloride formed (MgCl_2) neutralizes the contents of the duodenum with the formation of inabsorbable magnesium carbonate (MgCO_3) It is this that explains the laxative effect which develops when magnesium trisilicate is used over a lengthy period Magnesium trisilicate is nontoxic and is tolerated well It is administered orally in the form of a powder in a dosage of 0.5–1 g 2–3 times a day

Stored under ordinary conditions in well closed bottles

ACTIVATED CHARCOAL (Carbo activatus)

Black powder odourless and tasteless insoluble in the usual solvents Charcoal of animal or vegetable origin specially processed to give a large surface capable of adsorbing gases alkaloids toxins etc

Used in dyspepsia meteorism food poisoning and poisoning with alkaloids and the salts of heavy metals etc

Administered orally in cases of poisoning in a dose of 20–30 g in the form of a water suspension stomach lavage is also performed with a suspension of activated charcoal in water In cases of hyperacidity and meteorism 1–2 g in water is prescribed orally 3–4 times a day In poisoning a mixture of the following composition is also used activated charcoal—2 parts tannin and calcined magnesia—1 part each prescribed in the form of a suspension 2 tablets equivalent to 1 glass of warm water

Activated charcoal tablets (Tabulettae carbonis activati)

Synonyms Carbolon Carbolenum

Tablets containing 0.5 g activated charcoal More convenient to use than powdered activated carbon but has somewhat less adsorptive capacity since it contains fillers (up to 20% starch and sugar) which reduce the absorbing surface Chiefly used in meteorism and dyspepsia 1–3 tablets 3–4 times a day

III. ASTRINGENTS

A. Astringents of vegetable origin

TANNIN (*Tanninum*, *Acidum tannicum*)

Gallotannic acid Obtained from nutgalls (*Gallae turcicae*) excrescences on the young twigs of the Dyer's Oak of Asia Minor or from sumach found growing in the USSR *Rhus coriaria* L. and *Cotinus coggygria* Scop (*Rhus cotinus* L.), family *Anacardiaceae*

Light yellow or brownish yellow amorphous powder with faint characteristic odour and astringent taste very soluble in water and alcohol, insoluble in dry ether and chloroform Aqueous solutions form precipitates with alkaloids solutions of albumin and gelatine, and salts of heavy metals

Used as an astringent and antiphlogistic

The astringent action of tannin and other astringents is due to their ability of precipitating proteins with the formation of dense albuminates When applied to the mucous membranes or to a wound surface they cause partial coagulation of the proteins of the mucus or wound exudate thus forming a film which protects the sensory nerve endings of the underlying tissues from irritation. The resulting abatement of pain, local constriction of the vessels and limitation of secretion, as well as the direct consolidation of the cellular membranes lead to a diminution of the inflammatory reaction

Tannin is used in inflammatory processes in the oral cavity, nose pharynx and larynx in the form of a 1—2% aqueous or glycerine solution for rinsing or of a 5—10% ointment, in burns, ulcers, fissures and bedsores in the form of 3, 5 or 10% ointment or solutions in inflammatory diseases of the rectum and in colitis—enemas of 0.5—1% solutions Tannin is not administered orally as an antidiarrheic since it reacts first of all with the proteins of the gastric mucous membrane, when taken orally in large doses it causes loss of appetite and indigestion

Since tannin forms insoluble compounds with the salts of alkaloids and heavy metals it is often used in cases of oral poisoning with these substances, it is advisable to perform stomach lavage with a 0.5% aqueous solution of tannin It must be remembered that tannin forms unstable compounds with some alkaloids (*morphine*, *cocaine*, *atropine*, *nicotine*, *physostigmine*), for that reason they must be removed from the stomach by thorough lavage

Tannin is an ingredient of Novikov's antiseptic fluid and of the photo protective film proposed by D. I. Sorokina

To be stored in tightly closed bottles in a dry place

ALBUMIN TANNATE (*Albuminum tannicum*)

Synonym Tannalbin

Compound of tannin and albumin

Amorphous brownish powder almost insoluble in cold water and alcohol Unlike tannin, has no astringent action on the mucous membranes of the mouth and stomach Gradually hydrolyzed in the intestine, liberating free tannin which has an astringent effect

Used as an astringent in acute and chronic diseases of the intestine (diarrhea)¹ The dose for adults is 0.3, 0.5 or 1 g 3—4 times a day Children are prescribed 0.1—0.5 g, depending on their age. Often administered in combination with bismuth, benzonaphthol and salol ("Tansal") As a substitute for albumin tannate, thealbin can be used

Albumin tannate is to be stored in hermetically closed bottles

Tansal (*Tansalum*) Tablets containing 0.3 g albumine tannate and 0.3 g salol

¹ In infectious diseases of the intestine (including dysenteric diseases) albumin tannate and other astringents can only be used as adjuvants to specific methods of treatment

Used as an astringent and antiseptic in inflammatory diseases of the intestine (colitis enteritis) in a dosage of 1 tablet 3-4 times a day

Available in packets containing 6 tablets

THEALBIN (Thealbinum)

Compound of tea leaf tannin and casein

Amorphous brownish powder, almost insoluble in cold water and alcohol

Similar in action to albumin tannate, for which it is a substitute

Administered orally in a dosage of 0.3-0.5 g 3-4 times a day (for adults)

To be kept in hermetically closed bottles

OAK BARK (Cortex Quercus)

The bark of young branches and small trunks (up to 10 cm in diameter) of the English oak (*Quercus robur* L. *Q. pedunculata* Ehrh. or *sessiliflora* Salisb.), of the Beech family (Fagaceae) gathered in spring. Contains from 10 to 20% tannin

Used as an astringent in the form of a 10% decoction for gargling in gingivitis stomatitis and other inflammatory processes of the oral cavity the mouth pharynx and larynx. A 20% decoction is sometimes used for the treatment of burns

ST JOHN'S WORT HERB (Herba Hyperici)

Above ground parts of the common St John's Wort (*Hypericum perforatum*), family Guttiferae found growing throughout the USSR in Europe, the Caucasus Central Asia and Western Siberia gathered during the blooming period and dried

Contains tannin of the pyrocatechol type the flavonol glycoside hyperosid azulene volatile oil and other substances

Used orally as an astringent and antiseptic in colitis and externally for painting the gums and rinsing the mouth for the prevention and treatment of gingivitis and stomatitis. St John's Wort infusion is a substitute for rhatany infusion

BISTORT RHIZOME (Rhizoma Bistortae)

Rhizome of wild Bistort (*Polygonum bistorta* L.) a perennial herb of the Buckwheat family (Polygonaceae) gathered after the blooming period, freed of roots washed and dried

Contains 15-20% tannin gallic acid pigments starch and other substances

Used externally as an astringent in inflammatory diseases of the mucous membranes in the form of a decoction (10 g per 200 ml) or fluid extract (*Extractum Bistortae fluidum*)

POLYGONUM CARNEUM RHIZOME (Rhizoma Polygoni carnei)

Rhizome of *Polygonum carneum* a wild perennial herb of the Buckwheat family (Polygonaceae)

Used on a par with Bistort Rhizome

The fluid extract (*Extractum Polygoni carnei fluidum*) obtained by percolation with 70° alcohol is transparent reddish brown liquid. Administered orally as an astringent in acute and chronic colitis and enteritis in a dosage of 1/2-1 teaspoonful twice a day

To be kept in well closed containers in a place protected from light

BURNET RHIZOME AND ROOT (Rhizoma et radix Sanguisorbae)

Rhizome and root of the Common Burnet (*Sanguisorba officinalis* L.) family Rosaceae gathered in autumn and thoroughly washed and dried

Found growing throughout the entire territory of the USSR with the exception of the southern regions of Central Asia and the Caucasus. Contains tannin vitamin C and other substances

Decoctions and fluid extract (prepared with 70° alcohol) are used as astringent and hemostatic in diarrhea and hemoptysis and at times in uterine hemorrhage. A glass of boiling water is poured over a tablespoonful of chopped root and the decoction boiled 30 min cooled and strained. 1 tablespoonful is drunk 5-6 times a day

Sorbex Red sugar coated tablets contain 0.3 g of Burnet Root Extract. Used as an astringent and hemostatic in diarrhea and hemorrhage 1 tablet 3—4 times a day.

SAGE LEAF (Folia Salviae)

Dried leaves of cultivated Sage (*Salvia officinalis* L.) a perennial herb of the Mint family (Labiatae).

Contain tannin and volatile oil (approx 2%).

Used in the form of an infusion for rinsing the mouth and throat (a glass of boiling water is poured over one tablespoonful of leaves let stand 20 min cooled and strained).

WILD CHAMOMILE FLOWERS (Flores Chamomillae)

Flower heads of wild or cultivated Wild Chamomile (*Matricaria chamomilla* L.) and Matricary (*M. matricarioides* (Less) Porter *M. suaveolens* (Buchen) family Compositae) gathered at the beginning of blooming and dried. Contain volatile oil azulene (blue colour) anthemic acid a glycoside and other substances.

Azulene has antiphlogistic properties it also abates allergic reactions and intensifies regenerative processes. It has lately been established that apigenin (457 trihydroxyflavone) a substance isolated from Wild Chamomile, has a strong spasmolytic effect (Y. Rashkova and I. Yanku).

An infusion of Wild Chamomile Flowers prepared by steeping 1 tablespoonful in a glass of boiling water cooling and filtering is used orally and in enemas in intestinal spasms meteorism and diarrhea. It is also administered orally as a sudorific. Prescribed externally as a weak antiseptic and astringent gargle, lotion and bath.

ELDER FLOWERS (Flos Sambuci)

Dried flowers and flower buds of the European Elder (*Sambucus nigra* L.) Honeysuckle family (Caprifoliaceae). Contain volatile oil valeric acid and tannin.

Used orally as an astringent sudorific and diuretic also used externally for rinsing the mouth and for poultices.

Prescribed in the form of an infusion 1 tablespoonful is steeped 20 min in a glass of boiling water and strained. Dose $\frac{1}{4}$ glass 3—4 times a day 15 min before meals.

CINQUEFOIL RHIZOME (Rhizoma Tormentillae)

Rhizome of wild Cinquefoil (*Potentilla erecta* (L.) Hampe *P. tormentilla* Neck.) family Rosaceae dug in the autumn washed and dried.

Cinquefoil Rhizome contains a large amount of tannin as well as resin gum pigment and other substances.

Used in the form of a decoction chiefly in folk medicine administered orally in diarrhea and externally as a gargle in stomatitis gingivitis and angina.

B Salts of metals

a) Bismuth preparations

BISMUTH SUBNITRATE BASIC BISMUTH NITRATE (*Bismuthum subnitricum* *Bismuthi subnitratis* *Bismuthum nitricum basicum* *Magisterium bismuthi*)

Mixture of $\text{BiNO}_3(\text{OH})_2$, BiONO_3 and BiOOH .

White amorphous or fine crystalline powder insoluble in water and alcohol freely soluble in hydrochloric sulphuric and nitric acid.

Used as an astringent and to some extent as an antiseptic in gastrointestinal diseases (ulcer of the stomach and duodenum enteritis colitis).

Prescribed orally dosage for adults — 0.25—0.5 g 2—3 times a day children — 0.1 0.3 or 0.5 g. Applied externally in the form of ointments and dusting powders (5—10%) in inflammatory diseases of the skin and mucous membranes (dermatitis ulcers erosions eczema).

Available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well closed bottles in a place protected from light

Vicalin (Vicalinum) Tablets containing 0.35 g bismuth subnitrate, 0.4 g magnesium carbonate, 0.2 g sodium bicarbonate, 0.025 g powdered Calamus rhizome, 0.025 g powdered Buckthorn bark, 0.005 g rutin and 0.005 g khellin

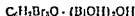
The tablets have an astringent, antacid and moderate laxative effect. The presence of rutin ensures a certain antiphlogistic action, and the khellin, a spasmolytic effect

Used in ulcer of the stomach and duodenum and in hyperacid gastritis. Administered orally, 1—2 tablets with half a glass of warm water 3 times a day after meals. The course of treatment is usually for 1—3 months, after a break of one month the course is repeated. During treatment patients must be kept on a diet.

The tablets usually cause no side-effects, at times the stool becomes more frequent, but this ceases when the dose is lowered. During treatment the faeces acquire a dark green or black colour.

BISMUTH TRIBROMOPHENATE (Bismuthum tribromophenatum)

Basic bismuth tribromophenate



Synonym Xeroform

Yellow, fine amorphous powder with faint characteristic odour, insoluble in water, alcohol, ether and chloroform. Contains 50—55% bismuth oxide.

Used externally in dusting powders and ointments (3—10%) as an astringent, drying and antiseptic agent.

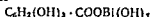
To be stored in well closed bottles in a place protected from light.

Bismuth tribromophenate ointment (Unguentum Bismuthi tribromophenati)

Composition: Bismuth tribromophenate 10 g, petrolatum 90 g. Yellow ointment of homogeneous consistency with characteristic odour.

BISMUTH SUBGALLATE (Bismuthum subgallicum)

Basic bismuth gallate



Synonym Dermatol

Lemon yellow powder without odour or taste, insoluble in water, alcohol and ether, dissolves with decomposition when warmed with mineral acids, freely soluble in sodium hydroxide, forming yellow solutions which quickly turn red in the air.

Contains 52—56.5% bismuth oxide.

Used externally as an antiseptic astringent and drying agent in inflammatory diseases of the skin and mucous membranes (ulcers, eczema, dermatitis) and in dusting powders, ointments and suppositories.

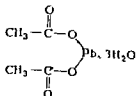
Available in powder form and in 10% ointment.

To be stored in well closed bottles.

b) Lead preparations

LEAD ACETATE (Plumbum aceticum)

Sugar of lead

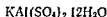


Colourless, transparent, glossy crystals or white crystalline accretions, faint acetic odour, freely soluble in water (1 : 25 in cold and 2 : 1 in boiling water)

Used externally in the form of 0.25–0.5% aqueous solutions as an astringent in inflammatory diseases of the skin and mucous membranes

To be stored in well closed bottles observing safety precautions (List B)
ALUMINIUM-POTASSIUM ALUM (Alumen, Aluminium sulfuricum cum Kalio sulfurico)

Aluminium potassium sulphate Contains 10.7% aluminium oxide



Colourless transparent crystals or white crystalline powder, efflorescent in air, soluble in water (1 : 10), freely soluble in hot water, insoluble in alcohol
The aqueous solution is acid with a sweetish astringent taste

Used externally as an astringent in the form of lotions and 0.5–1% aqueous solutions for gargling, washing and syringing in inflammatory diseases of the mucous membranes and skin. Also used in the form of pencils for cauterizing in trachoma and as a hemostatic for cuts (when shaving)

To be kept in well closed bottles

STYPTIC PENCILS Composition Aluminium potassium alum 20%, aluminium sulphate 78%, calcium oxide 2%

White cylindrical sticks, dissolve in water forming acid solution of astringent taste

Used for stopping the flow of blood in small cuts and abrasions after shaving

BURNT ALUM (Alumen ustum)

Burnt alum is obtained by heating aluminium potassium alum at a maximum temperature of 160° until 55% of the initial weight remains. The residual mass is ground to a powder and sifted

White powder, slowly and incompletely dissolves in water (1 : 30), slowly absorbs moisture from the air

Used in dusting powders as an astringent and drying agent (for excessive sweating of the feet, etc.)

To be kept in well closed bottles

IV. AGENTS WHOSE ACTION IS CHIEFLY ASSOCIATED WITH IRRITATION OF THE NERVE ENDINGS OF THE SKIN, MUSCLES AND MUCOUS MEMBRANES

A. Agents containing volatile oils

PEPPERMINT LEAF (Folia Menthae piperitae)

Dried leaves of cultivated Peppermint (*Mentha piperita*), a perennial herb of the family Labiatae. Contain volatile oil (at least 1%) of which menthol is a constituent

An infusion of Peppermint Leaf (5 g per 200 ml) is used orally for nausea and as a choleric. Peppermint Leaf is also an ingredient of choleric tea

BOROMENTHOL (Boromentholum) Ointment of the following composition
menthol 0.5 parts, boric acid 5.4 parts, petrolatum 94.1 parts

Used as an antiseptic and analgesic for spreading on the skin in pruritus and neuralgia, and also for application to the mucous membrane of the nose in coryza

Available in metal tubes containing 5 g

Pectussin (Pectusinum) Tablets of the following composition
menthol 0.004 g, eucalyptus oil 0.0005 g, talc 0.03 g, sugar 0.75 g

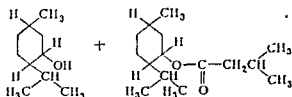
Used in inflammatory diseases of the upper respiratory passages To be held in mouth until completely absorbed

Ingacant — pocket inhaler containing a piece of cloth impregnated with a mixture of the following composition camphor 0.3 g, menthol 0.17 g; methyl salicylate 0.08 g, eucalyptus oil 0.1 g

Used for inhalation in acute rhinitis (see also Ingaphen)

MENTHYL VALERATE (*Menthylum valericum*)

25—30% solution of menthol in menthyl isovalerate



Synonym **Validol**

Colourless transparent oily liquid with odour of menthol, very freely soluble in alcohol insoluble in water

Similar to menthol in its action Has a sedative influence on the central nervous system, also has a reflex vasodilator effect

Prescribed in doses of 4—5 drops in stenocardia, neuroses and hysteria, also used as an antemetic in seasickness and airsickness It is recommended that the preparation should be applied to a piece of sugar, and the latter held in the mouth till completely dissolved Also available in the form of tablets containing 0.06 g menthyl valerate (3 drops) and sugar

Menthyl valerate is used locally in the form of a 5—10% alcoholic solution for the relief of itching skin

To be stored in well stoppered bottles in a cool place

Rp *Menthylu valericu* 50

DS 5 drops on a piece of sugar

EUCALYPTUS LEAF (*Folia Eucalypti*)

Dried leaves gathered from mature branches of the Blue gum tree (*Eucalyptus globulus* Labill.) and the Ash Grey Eucalyptus (*E. cinerea* Mull.), family Myrtaceae, cultivated along the Black Sea coast of the USSR and in the south of the Soviet Ukraine

Contain volatile eucalyptus oil (25%) esters, organic acids, tannin and other substances

Eucalyptus decoctions and tincture, and eucalyptus oil are used as antiseptics for gargling and inhalation in diseases of the upper respiratory passages, as well as for the treatment of fresh and infected wounds and inflammatory diseases of the female genitalia (lotions and washes)

The tincture is sometimes prescribed orally as a sedative

Eucalyptus Tincture (*Tinctura Eucalypti*) 20% tincture prepared with 70° alcohol transparent, greenish brown liquid with characteristic odour

CAPSICUM TINCTURE (*Tinctura Capsici*) Transparent red liquid of burning taste

Used orally to increase the appetite and improve digestion (up to 10—20 drops) and externally as a skin irritant

Compound Capsicum Liniment Composition Capsicum tincture 10 parts, green soap 20 parts water 23 parts, 96° alcohol 57 parts, ammonia water 100 parts

Used externally for rubbing on the skin

Frostbite Ointment Composition Capsicum tincture 77 parts, formic acid 0.32 part, 25% ammonia water 14 parts, camphorated oil 64 parts, alcoholic solution of green soap 3.5 parts, castor oil 1 part anhydrous lanolin 1 part, lard 975 parts, yellow petrolatum 72 parts

B Agents containing dichlorodiethyl sulphide and other vesicants

PSORIASIN (Psoriasinum)

Ointment containing 1 part chemically pure dichlorodiethyl sulphide to 20,000 parts of petrolatum

Dichlorodiethyl sulphide, or mustard gas, is a vesicant. On coming in contact with the skin causes effects of diverse degree—from mild erythema to the formation of vesicles with subsequent ulceration and necrosis of the tissues (depending on the concentration, duration of action, individual sensitivity, etc.) Severe effects occur when dichlorodiethyl sulphide comes in contact with the mucous membranes especially the mucous membrane of the eye. The local action of mustard gas is accompanied by general resorptive toxic manifestations.

Dichlorodiethyl sulphide has been proposed in very great dilution (1:20,000) for the treatment of psoriasis. The mode of action is not sufficiently clear. It may be that the therapeutic effect is due to a certain extent to the reaction between dichlorodiethyl sulphide and the proteins of the skin, as well as to inhibition of the enzyme systems and an influence on the receptors of the skin.

Psoriasin is used in the treatment of chronic forms of psoriasis not in a stage of exacerbation and without substantial distribution of the process.

Treatment must be carried out with caution.

Before commencing the systematic use of psoriasin the sensitivity of the patient's skin is determined. This is done by spreading the ointment on a limited effected area for 3—4 days. If the preparation is tolerated well, systematic application is begun. In cases of heightened sensitivity of the skin the use of psoriasin is impermissible. It must be remembered that heightened sensitivity to psoriasin (as well as to antipsoriaticum) may develop during treatment.

Method of use. The ointment is rubbed lightly on all foci of affection (the way the hair grows) with the exception of the lids, once a day for 6 days. On the 7th day a break is made in treatment, the patient is given a bath with soap and changes his underclothes. The next day application of the ointment is recommenced. 2—4 such cycles of treatment are given. If psoriatic eruptions disappear sooner, no more applications are given. Dry bandages are applied to hands and feet, forearms and legs after rubbing in the ointment, and are changed once a week after bathing. Wax paper may be applied to markedly infiltrated scales after rubbing in. It is not advisable to apply the ointment to tender areas of the skin (the armpits, under the mammary glands in women, the groins and anal region).

Treatment with psoriasin should be carried out under a physician's observation. Before and during treatment the blood and urine are examined (once a week). When spreading the ointment on foci of affection on the face and the hairy part of the head, it must not be allowed to come in contact with the lids and eyes.

The use of psoriasin is contraindicated in affections of the parenchyma of the liver and kidneys; the ointment must not be applied to moist sections of the skin. Psoriasin must also not be used if there are manifestations of irritation of the skin along with psoriatic eruptions.

Psoriasin is contraindicated for repeated use if heightened sensitivity to the preparation was observed following the preceding application.

Pigmentation usually appears on areas treated with psoriasin; this disappears in 1—3 weeks or longer, after application of the ointment is discontinued.

Available in bottles of 100 g. To be dispensed only on a physician's prescription, and not in excess of 100 g. Repeated dispensation permissible only on presentation of a new prescription. To be kept locked (List A) in a cool place. Great caution must be observed when preparing psoriasin and when working with it.

ANTIPSORIATICUM

Ointment containing 1 part chemically pure trichlorotriethylamine per 40 000 (or 100 000) parts of petrolatum or autol ointment.

Trichlorotriethylamine ("nitrogen mustard gas") is also a vesicant which like psoriasin has been proposed in great dilution for the treatment of psoriasis.

Before beginning systematic treatment the sensitivity of the patient's skin to the preparation is determined. If it is tolerated well systematic application of the ointment is commenced.

The method of use, duration of treatment, contraindications and precautionary measures are the same as for psoriasin.

Available in bottles of 100 g.

To be kept locked (List A) in a cool place.

Regulations for dispensing are the same as for psoriasin.

C. Agents containing aliphatic hydrocarbons

NEOBENZINOL (Neubenzinolum)

Mixture of aliphatic hydrocarbons and olive or persic oil. Contains 16% n hexane, 16% n heptane and 68% oil. Transparent, light yellow liquid with odour of petrol.

Used as a nonspecific desensitizing agent in bronchial asthma and scrofuloderma. Administered intramuscularly, 0.6—0.8 ml in bronchial asthma and 0.2—0.3 ml in scrofuloderma. In bronchial asthma, neobenzinol is given during frequent attacks; it is not prescribed for preventive purposes in the absence of attacks. Usually one or two injections, the second 2½—3 weeks after the first, are sufficient. The injection is repeated only if the first gave no effect or if attacks of choking recommence after some time. In scrofuloderma injections are repeated at intervals of 2—3 weeks. The day after an administration, a painful infiltrate develops at the site of injection; a general reaction is likewise observed—elevation of the temperature and deterioration in subjective feeling. These symptoms are associated with the therapeutic action of the preparation, which is based on so called "irritation therapy".

Neobenzinol is contraindicated in active tuberculosis, febrile reactions and cardiac asthma.

Available in ampoules of 0.4 ml. Ampoules are to be opened immediately before use.

To be kept in a cool place protected from light and remote from flames.

D Bitters

BITTER TINCTURE (Tinctura amara)

Composition: Centaury Herb 60 parts, Buck Bean Leaf 60 parts, Calamus Root 30 parts, Wormwood Herb 30 parts, Orange Peel 15 parts, sufficient 40° alcohol to prepare one liter of tincture by the percolation method. Transparent brownish liquid with bitter spicy taste and aromatic odour.

Administered orally, 10—20 drops 2—3 times a day, 15—30 min before meals to increase the appetite and improve digestion.

The effect of the tincture like that of other bitters, is due to reflex intensification of the secretion of gastric juice following irritation of the endings of the taste nerves in the mouth.

GENTIAN ROOT (Radix Gentianae)

Rhizome and root of the Yellow Gentian (*Gentiana lutea*), family Gentianaceae, dug in the autumn and quickly dried. Contains gentiopicrin, a crystalline bitter principle.

Used for the preparation of Gentian extract and tincture

Thick Gentian Extract (*Extractum Gentianae spissum*) Thick reddish brown extract, faint characteristic odour, extremely bitter taste Dissolves in water with the formation of an almost transparent acid solution

Used as an ingredient of pills

Gentian Tincture (*Tinctura Gentianae*) 20% tincture prepared with 40° alcohol Transparent yellowish brown liquid with characteristic odour and extremely bitter taste Forms transparent solutions with water

Prescribed as bitters for increasing the appetite and improving digestion

Dosage 20—30 drops 2—3 times a day, 15—30 min before meals, alone or in combination with other bitters

CENTAURY HERB (*Herba Centaurii*)

Above ground parts of Centaury (*Centaureum umbellatum* Gilib, *Erythraea centaureum* Pers), a biennial herb of the family Gentianaceae, gathered during the blooming period

Used in the form of infusions, decoctions and tinctures as bitters An ingredient of Bitter Tincture

WORMWOOD HERB (*Herba Absinthii*)

Leaves and blooming leafy tops of wild Wormwood (*Artemisia absinthium* L.), a perennial herb of the family Compositae gathered before or during the blooming period

Contains the glycosides absinthin and anabsinthin, volatile oils, vitamin C tannin and other substances

Used in the form of tincture, infusion and extract as bitters for arousing the appetite and intensifying the activity of the digestive organs One of the ingredients of Bitter Tincture

Thick Wormwood Extract (*Extractum Absinthii spissum*) Aqueous extract of Wormwood Herb Thick dark brown mass with aromatic wormwood odour and bitter taste, forms a transparent solution with water

Wormwood Tincture (*Tinctura Absinthii*) 20% tincture prepared with 70° alcohol Transparent brownish green liquid with characteristic odour and very bitter taste

BUCK BEAN LEAF (*Folia Menyanthis*) Marsh trefoil

Buck Bean (*Menyanthes trifoliata* L.) family Menyanthaceae, fully developed leaves with petioles broken off short

Grows throughout almost all the European part of the USSR in bogs and along the banks of rivers and the shores of lakes Contains bitter glycosides and other substances

Used in the form of an infusion as bitters for arousing the appetite 2 teaspoonfuls are steeped in a glass of boiling water, and strained off, $\frac{1}{4}$ glass is drunk 2—3 times a day half an hour before meals An ingredient of Choleric Tea and Bitter Tincture

Rp Inf fol Trifolii 100 2000

DS 1 tablespoonful 2—3 times a day before meals

DANDELION ROOT (*Radix Taraxaci*)

Roots of the wild Dandelion (*Taraxacum officinale* Wigg), a perennial herb of the family Compositae the roots are dug in the autumn and dried Contain a bitter glycoside and up to 40% inulin

Used as bitters for arousing the appetite, also used as a laxative and choleric. A teaspoonful of finely chopped root is steeped in a glass of boiling water like tea, let stand 20 min, cooled and strained, $\frac{1}{4}$ glass is drunk 3—4 times a day half an hour before meals

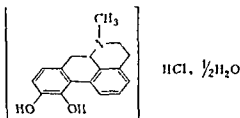
Thick Dandelion Extract (*Extractum Taraxaci spissum*) Thick brown extract, soluble in water with the formation of a slightly turbid solution

Used as an ingredient of pills

V. EMETICS AND EXPECTORANTS

APOMORPHONE HYDROCHLORIDE (Apomorphinum hydrochloricum, Apomorphini hydrochloridum)

Obtained synthetically from morphine by heating with hydrochloric acid water is split off and partial molecular rearrangement takes place



White slightly greyish or slightly yellowish crystalline powder odourless turns green on exposure to air or light sparingly soluble in water (1:60) and alcohol (1:50) almost insoluble in ether and chloroform

Solutions quickly turn green under the influence of light and air and lose their potency

Solutions are prepared ex tempore using 0.001 N hydrochloric acid as a solvent they are sterilized by Tyndallization

Apomorphine has a selective stimulating influence on the emetic centre.

Chiefly used as an emetic for the rapid removal of poisonous substances and spoiled foodstuffs from the stomach especially when it is impossible to perform stomach lavage. The drug acts within a few minutes after subcutaneous injection. Adults are given injections of 0.002–0.003 g (0.2–0.5 ml 1% solution) children over two years old—0.001–0.003 g. Rarely used as an expectorant because of the transitory nature of the effect. Usually prescribed for this purpose in mixtures: adults—0.001–0.005 g children from 2 to 5 years old—0.0005–0.001 g from 6 to 12 years—0.0012–0.0025 g

Apomorphine is likewise used for creating a conditioned reflex reaction (repugnance) toward alcohol in the treatment of patients with chronic alcoholism. Patients are given subcutaneous injections beginning with 0.2 ml 1% solution and gradually raising the dose 0.1 ml until the individual dose causing emesis is reached

Apomorphine solution is sometimes given subcutaneously in acute alcoholic intoxication. The drug often has a sedative effect before emesis followed in 5–30 min by sleep

Maximal doses for adults: single orally—0.001 g subcutaneously—0.005 g daily orally—0.03 g subcutaneously—0.01 g

Maximal doses for children: a) orally (as an expectorant) 2 years old single—0.001 g daily—0.003 g 3–4 years single—0.0015 g daily—0.0045 g 5–6 years single—0.002 g daily—0.006 g 7–9 years single—0.0025 g daily—0.0075 g 10–14 years single—0.003 g daily—0.009 g b) subcutaneously (as an emetic) single injections 2 years old—0.002 g 3–4 years—0.0025 g 5–9 years—0.003 g 10–14 years—0.003–0.004 g. Apomorphine is not prescribed for infants up to 2 years old

Contraindications to the use of apomorphine: serious heart disease atherosclerosis open forms of pulmonary tuberculosis ulcer of the stomach and duodenum burns of the stomach with strong acids and alkalis organic diseases of the central nervous system old age. Apomorphine does not act when the patient is in a state of deep narcosis; this is due to depression of the emetic centre

Available in powder form

To be kept locked (List A) in well closed bottles of amber glass

THERMOPSIS HERB (Herba Thermopsidis) (List B)

Above ground parts of wild Thermopsis (*Thermopsis lanceolata* R Br), perennial herb of the family Leguminosae, gathered from the beginning of blooming till the formation of fruit, and dried Habitat the Trans Volga region, Siberia, Kazakhstan and other parts of the USSR Contains alkaloids (cytisine, methylcytisine, pachycarpine, anagyrine, thermopsine, thermopsidine), saponins, volatile oil and other substances Should contain not less than 1% total alkaloids

The plant and the individual substances contained in it have a complicated effect on the body Cytisine and to less degree methylcytisine, stimulate respiration and raise the blood pressure (see Cytiton), pachycarpine has a depressing influence on the ganglia of the autonomic division of the nervous system (see Pachycarpine)

The plant as a whole acts as an expectorant, and in large doses as an emetic

Used in the form of infusions, powder and dry extract as an expectorant it is to some extent a substitute for ipecacuanha preparations

Dosage for adults powder—0.01—0.05 g 2—3 times a day, infusion (0.6—1 g to 180—200 ml)—1 tablespoonful 3—4 times a day Dosage for children from 4 to 12 months old—1 teaspoonful of infusion (0.12 g per 100 ml) 3—5 times a day, older children—1 teaspoonful—1 dessertspoonful of infusion (0.2 g per 100 ml)

Maximal doses of Thermopsis Herb for adults single—0.1 g, daily—0.3 g

Maximal doses for children up to 1 year old single—0.005 g, daily—0.015 g, 2 years single—0.01 g daily—0.03 g 3—4 years single—0.015 g daily—0.045 g, 5—6 years single—0.02 g daily—0.06 g 7—9 years single—0.025 g, daily—0.075 g, 10—14 years single—0.03 g daily—0.1 g

Dry Thermopsis Extract (*Extractum herbae Thermopsidis siccum*) Mixture of dry standardized Thermopsis extract and lactose 1 g is the equivalent of 1 g Thermopsis Herb with an alkaloid content of 1% Light brown powder freely soluble in water

Prescribed in dosage of 1 tablet 2—3 times a day

Available in powder form and in tablets of 0.05 g

ALTHEA ROOT (*Radix Althaeae*) Marshmallow root

Root of wild and cultivated Althaea (*Althaea officinalis* L and *Althaea armeniaca* Ten), perennial herbs of the Mallow family (Malvaceae) the roots are dug in the autumn washed, freed of the cork layer and dried Contain much mucilage

Used in the form of powder, infusion and syrup as an expectorant and antiphlogistic, for the most part in diseases of the respiratory passages

Dry Althae Root Extract (*Extractum Althaeae siccum*) Greyish yellow powder, almost odourless, characteristic sweetish taste

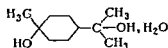
POLYGALA ROOT (*Radix Polygalae*)

Root of wild Milkwort (*Polygala tenuifolia* Willd and *P. sibirica* L) perennial herbs of the family Polygalaceae, dug in the autumn and dried

Contains saponins whose action is similar to that of the saponins of Senega root The saponin content is approximately 40% of the saponin content of Senega

Acts as a potent expectorant, and in the proper doses fully replaces Senega

TERPIN HYDRATE (*Terpinum hydratum*)



Made by the action of sulphuric acid on the pinene fraction of turpentine

Colourless transparent crystals of white crystalline powder odourless slightly bitterish taste sparingly soluble in water (1:250 in cold water and 1:31 in boiling water) soluble in alcohol (1:10) Melting point 115—117°

Administered orally either alone or in combination with other preparations as an expectorant (in chronic bronchitis) Dosage for adults 0.25—0.3 g Dosage for children 0.05—0.25 g depending on the age

Available in powder form and in tablets of 0.2 and 0.5 g as well as compound tablets containing codeine and sodium bicarbonate

SODIUM BENZOATE (Natrium benzoicum)



White granular or crystalline powder sweetish salty taste freely soluble in water (1:2) sparingly soluble in alcohol (1:45) Solutions are weakly alkaline

Used orally as an expectorant in bronchitis and other diseases of the respiratory passages administered in powders and solutions (usually in mixtures) Adults are given 0.2—0.5 g 3—4 times a day Children up to 1 year old are given doses of 0.03—0.05 g 2—5 years—0.05—0.1 g 6—12 years—0.015—0.3 g

Also administered intravenously (15% solution) in pulmonary abscess and purulent bronchitis

Sodium benzoate has likewise been proposed for testing the antitoxic function of the liver. The method is based on the fact that the aminoacetic acid (glycine) formed in the liver combines with the benzoic acid administered thus forming hippuric acid. The functional condition of the liver can be assessed by the amount of hippuric acid excreted in the urine.

4 g of the drug is administered orally (A. Y. Pitel). The excretion of 37 g sodium benzoate in the form of hippuric acid is taken as 100% liver function. In healthy people the percentage may range from 70 to 100.

Sodium benzoate can also be administered intravenously for testing the liver function (1.77 g in 30 ml twice distilled water). The excretion of 14 g is taken as 100%.

GUAIACOL CARBONATE Duotal (Guajacolum carbonicum Duotalum)

White odourless crystalline powder or needles insoluble in water sparingly soluble in cold alcohol and ether Melting point 85—88°

Administered orally in place of guaiacol in chronic inflammatory diseases of the respiratory passages (bronchitis bronchoectasia) Dosage for adults 0.3—0.5 g 2—3 times a day Dosage for children up to 1 year old—0.03—0.05 g 2—5 years—0.1—0.25 g 6—12 years—0.25—0.4 g

Available in powder form and in tablets of 0.3 g

To be stored in well closed bottles of amber glass

JACOBS LADDER RHIZOME AND ROOT (Rhizoma cum radicibus Polemonii coerulei)

Jacob's Ladder perennial herb of the family Polemoniaceae grows throughout the entire territory of the USSR. The plant particularly the rhizome and roots contains saponins. Acts as an expectorant and sedative. Used as an expectorant in acute and chronic bronchitis sometimes administered in combination with Gnaphalium in ulcer of the stomach. As an expectorant an infusion of the roots is prescribed (6—8 g per 200 ml) or a decoction (3—6 g per 200 ml) 3—5 tablespoonfuls a day after meals also prescribed in the form of tablets of 0.2 g.

In ulcer of the stomach a decoction is prescribed 1 tablespoonful 3 times a day after meals along with Gnaphalium infusion (10 g per 200 ml)

3 tablespoonfuls 3 times a day before meals Also available in the form of tablets containing dry extracts of Jacob's Ladder root and Gnaphalium herb

LICORICE ROOT (*Radix Liquiritiae* *Radix Glycyrrhizae*)

Dried roots and over ground shoots of *Glycyrrhiza glabra* L. and *Glycyrrhiza uralensis* Fisch., family Leguminosae, freed of cork

In medicine, entire cleaned roots cut into cubes are used, as well as powder (*Pulvis radicis Glycyrrhizae*) Contain the glycoside glycyrrhizin, carbohydrates, mucilage and other substances It has lately been established that on hydrolysis glycyrrhizin yields glycyrrhetic acid, which has antiphlogistic properties Spasmolytic substances have also been isolated from Licorice Root, liquiritoside (a flavanone glycoside) and 2,4,4'-trihydroxychalcone.

Dry Licorice Root Extract (*Extractum Glycyrrhizae* (*Liquiritiae*) *siccum*)
Brownish yellow fine dry powder with faint characteristic odour and insipid sweet taste, soluble in water with the formation of a transparent foamy solution

PLANTAIN LEAF (*Folia Plantaginis majoris*)

Dried leaves of the common Plantain (*Plantago major* L.), family Plantaginaceae, a perennial herb which grows throughout the entire territory of the USSR

Contain the glycoside rhananthin carotene, vitamin C, bitter principles and tannin

Used in the form of an infusion as an expectorant (1 tablespoonful of chopped leaves is steeped 15 min in a glass of boiling water and strained off, 1 tablespoonful is taken 3—4 times a day The juice from fresh Plantain leaves is used as bitters)

Plantain Juice (*Succus Plantaginis*) Mixture of juice from the fresh leaves of *Plantago major* and the above ground parts of *P. psyllium* preserved with 20% alcohol

Administered in an acid gastritis and chronic colitis, 1 tablespoonful 3 times a day, 15—30 min before meals Course of treatment 30 days

MOTHER-OF-THYME HERB (*Herba Serpylli*)

Dried above ground parts of *Thymus serpyllum* L., a perennial subshrub of the Mint family (Labiatae) Grows throughout the entire European part of the USSR, in Siberia and the Caucasus Contains volatile oil (up to 1%), tannin, bitter principles and other substances

Used orally in the form of a decoction and fluid extract as an expectorant, and also as an analgetic in radiculitis and neuritis

The extract is an ingredient of "Pertussin

PERTUSSIN (*Pertussinum*)

Composition Mother of Thyme Extract or Thyme Extract 12 parts, potassium bromide 1 part, sugar syrup 82 parts 95° ethanol 5 parts

Brown syrup like liquid with aromatic odour and slightly salty taste.

Used as an expectorant cough remedy in bronchitis and other diseases of the upper respiratory passages

Also prescribed for children with whooping cough

Dosage for adults 1 tablespoonful 3 times a day Dosage for children from 1/2 teaspoonful to 1 dessertspoonful

WILD ROSEMARY HERB (*Herba Ledii palustris*)

Dried above ground parts of the Wild Rosemary (*Ledum palustre* L.), Heath family (Ericaceae) Contains volatile oil (thick green oil with characteristic odour, from which "ledum camphor", a solid substance, has been isolated), arbutin, tannin, and other substances

Used as an expectorant, and externally (boiled with oil) in skin diseases

Caution must be observed when using Wild Rosemary since it has been reported that the plant is poisonous

WILD MARJORAM HERB (*Herba Origanii*)

Dried above ground parts of the Wild Marjoram (*Origanum vulgare* L.) Mint family (Labiatae) found growing in dry open places in the steppe zone of the European part of the USSR. Contains volatile oil, tannin and other substances.

Used orally in alony of the intestine and as an expectorant used externally for baths.

COLTS FOOT LEAF (Folium Farfarae)

Dried leaves of wild Colts foot (*Tussilago farfara* L.) a perennial herb of the family Compositae. The leaves are gathered during the first half of summer. Contain a glycoside (tussilagin), inulin, volatile oil, tannin, mucilage and other substances. Used as an expectorant.

SOAPROOT (Radix Saponariae)

Dried chopped root of *Saponaria officinalis* L. Pink family (Caryophyllaceae), found throughout the USSR. Contains considerable saponins (approx 5%).

Used orally in the form of a cold infusion or decoction as an expectorant in bronchitis and other diseases of the respiratory passages.

INULA RHIZOME AND ROOT (Rhizoma et radix Inulae helenii)

Rhizome and root of Elecampine (*Inula helenium* L.) family Compositae found growing in damp places throughout almost the entire territory of the USSR. Contains saponins and volatile oil (of which alantolactone and isovalantolactone are constituents), mucilage and bitter principles. Used as an expectorant.

PINE BUDS (Gemmae Pini)

Contain resin, volatile oil, a bitter principle (pinoplicrin), tannin, vitamin C, starch, mineral salts and other substances.

Used in the form of a decoction (10 g per 200 ml) as an expectorant. Diuretic and antiseptic infusions are used for inhalation in inflammatory diseases of the upper respiratory passages.

VI LAXATIVES

A Vegetable laxatives containing anthraglycosides

RHUBARB (Rheum palmatum L. var tanguticum Maxim)

Perennial herb of the Buckwheat family (Polygonaceae) in medical practice the bark free rhizome and roots of Tangut Rhubarb (*Radix Rhei*) which is cultivated in the USSR are used.

Rhubarb rhizome and roots contain 3—6% anthraglycosides, 6—12% tanoglycosides, chrysophanic acid, resins, pigments and other substances.

Anthraglycosides are ether like compounds which after sugar is split off form emodin (rheoemodin or trihydroxymethylanthraquinone) and other derivatives of anthraquinone.

The chief active principles are emodin and chrysophanic acid which are formed in the intestine from the anthraglycosides and are also contained partially in the free form in Rhubarb. They irritate the interoreceptors of the intestine and cause an intensification of peristalsis chiefly affecting the large intestine and causing its more rapid evacuation. The laxative effect sets in within 8—10 hours after administration of Rhubarb preparations.

The slow effect and the predominant influence on the large intestine are usually explained as being due to the fact that the cleavage of the anthraglycosides in the intestine takes place slowly and that the accumulation of sufficient active principles for a laxative effect takes place only when the large intestine is reached. According to other findings (I. V. Mozgov) the receptors of the large intestine are the most sensitive and react to concentrations of emodin that have no effect on the receptors of the small intestine besides this.

after emodin is absorbed in the small intestine it is excreted by the large intestine intensifying its peristalsis

Rhubarb is used in the form of powders pills and decoctions either alone or in combination with other substances as laxatives chiefly in chronic (habitual) constipation They are usually administered before retiring Rhubarb preparations are tolerated well and do not upset the absorption process and normal activity of the small intestine

The resinous substances contained in the plant may have a somewhat irritating effect on the intestine

Rhubarb preparations are sometimes used in small doses (0.05–0.2 g) as astringents that diminish intestinal peristalsis Their astringent effect is due to the presence of tannoglycosides which form a precipitate with proteins in this way protecting the receptors of the mucous membrane of the intestine

When Rhubarb preparations are taken the urine sweat and milk assume a yellow colour due to the presence of chrysophanic acid on the addition of alkali this changes to red (formation of hydroxymethylanthraquinones)

The following Rhubarb preparations are used

Rhubarb Powder (*Pulvis radicis Rhei*) Yellowish orange or red powder crunches on the teeth due to the presence of calcium oxalate crystals

Prescribed in powders tablets and pills Single doses for adults 0.5–2 g Children 0.1–1 g

Dry Rhubarb Extract (*Extractum Rhei siccum*) Aqueous alcoholic extract Small porous lumps or coarse powder of yellowish brown colour characteristic odour and bitterish taste Gives a slightly turbid acid solution with water Single dose 0.1–1 g

Bitter Rhubarb Alcoholic Tincture (*Tinctura Rhei amara spiritulosa*) Obtained from powdered Rhubarb rhizome and roots (80 g) Gentian root (20 g), Calamus root (10 g) and enough 70° alcohol to give 1 liter of tincture Transparent dark brown or red liquid characteristic aromatic odour and bitter taste

Used in atony of the intestine and meteorism and also to improve the digestion Dosage $\frac{1}{2}$ –1 teaspoonful twice a day before meals

BUCKTHORN BARK (*Cortex Frangulae*)

Dried bark of branches and trunks of the Alder Buckthorn (*Frangula alnus* Miller) gathered in early spring bush of the family Rhamnaceae which grows in the forest zone of the European part of the USSR and in Western Siberia

Contains up to 5% anthraglycosides closely related to the anthraglycosides of Rhubarb saponins tannin and other substances

Similar to Rhubarb in its action

Administered orally in the form of decoctions extracts and pills as a mild laxative The effect sets in within 8–10 hours after taking

Buckthorn Bark is used in the following way a glass of boiling water is poured over 1 tablespoonful of bark and boiled 20 min the decoction is strained off cooled and drunk in a dose of half a glass before retiring and in the morning

Fluid Buckthorn Extract (*Extractum Frangulae fluidum*)

Dark brown fluid extract of bitter taste gives turbid solution with water

Prescribed as a laxative in doses of 20–40 drops

Dry Buckthorn Extract (*Extractum Frangulae siccum*)

Small lumps or powder of brown colour slight characteristic odour bitterish taste

Available in sugar coated tablets of 0.2 g 1–2 tablets are taken before retiring

IMERETIN BUCKTHORN (*Rhamnus Imeretinae*)

A decoction and a fluid extract from the bark are used

The decoction is prepared by pouring $1\frac{1}{4}$ glass of boiling water over 2 tablespoonfuls of powdered bark boiling 20 min cooling and straining 1 glass of decoction is obtained to be taken in dosage of $\frac{1}{4}$ glass night and morning

A fluid extract is prepared from the bark by percolation with 40° alcohol, reddish brown liquid of bitter taste

Prescribed in habitual constipation 2 teaspoonfuls before retiring (for adults) If the effect is inadequate the dose can be increased to 3 teaspoonfuls (not more!) The action is similar to that of Alder Buckthorn

B. Laxative salts

SODIUM SULPHATE (Natrium sulfuricum), Glauber's salt $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$

Colourless transparent efflorescent crystals, bitter salty taste, freely soluble in water (1:3 in cold water and 3:1 at 33°), insoluble in alcohol, dissolves in its water of crystallization on heating

Administered orally as a laxative The laxative effect of sodium sulphate, like that of other laxative salts, is chiefly due to its slow absorption from the intestine and the change in the osmotic pressure the drug causes the accumulation of water in the intestine the contents of the intestine are thinned, peristalsis is intensified and the fecal mass is evacuated more rapidly

A certain role is likewise played by the irritation of the receptors in the mucous membrane of the intestine by the salt solutions

Unlike vegetable laxatives containing anthraglycosides, salt laxatives act throughout the entire length of the intestine The effect usually sets in within 4–6 hours after taking the drug

The dosage of sodium sulphate for adults is 15–30 g, for children, 1 g for each year of their age The salt is taken on an empty stomach in $\frac{1}{2}$ –1 glass of water

ARTIFICIAL CARLSBAD SALT (Sal carolinum facilius)

Composition sodium sulphate 22 parts sodium bicarbonate 18 parts, sodium chloride 9 parts potassium sulphate 1 part

Dry white powder soluble in water (1:40) with the formation of a colourless solution

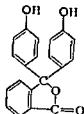
1 teaspoonful of this mixture (5–6 g) dissolved in 1 liter of water is a substitute for natural alkaline Glauber's salt water

Used as a laxative in a dosage of from 1 teaspoonful of the powder for children 2–6 years old to 1 tablespoonful for adults

C. Phenolphthalein group

PHENOLPHTHALEIN (Phenolphthaleinum)

Condensation product of phthalic anhydride and phenol



Synonyms Laxatol Laxoin Laxone Phenaloin Purgyl, Thalinal

White or slightly yellowish fine crystalline powder, odourless and tasteless, almost insoluble in water, soluble in alcohol (1:12)

Similar to the anthraglycosides in the character of its laxative effect like them it acts chiefly on the large intestine

Used in chronic constipation

Single doses for adults 0.1–0.2 g (up to 0.3 g a day), single doses for children (over 2 years old) 0.03–0.1 g depending on the age

Phenolphthalein should not be prescribed for lengthy periods since it possesses cumulative properties and has an irritating effect on the kidneys

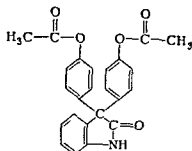
Phenolphthalein tablets (Purgen) (Tabulettae phenolphthaleini Purgenum)

Tablets containing 0.05 g phenolphthalein (for children) and 0.1 g (for adults)

1 tablet is given 1–3 times a day

ISAPHENIN (Isapheninum)

Diacetyl diphenolisatin



Synonyms Acetalax Acetphenolisatin Astil Bisatin Cirotil Diphesatine Disacetine Ditin Isazen Isocrin Laxaseptol Laxyl Novolax Prulax Purgaceen Purgophen Regal

Light white powder with faint acetic odour insoluble in water sparingly soluble in alcohol

Has a laxative effect similar in properties to phenolphthalein but less toxic does not cause irritation of the kidneys and has a more powerful laxative action Hydrolyzed by the alkaline contents of the intestine with the formation of dihydroxyphenylisatin which has a laxative effect

Used orally as a laxative in habitual constipation and atony of the intestine

Adults are prescribed 0.01–0.015 g (1–1½ tablets) twice a day or a single dose of 0.02 g (2 tablets) Older children are prescribed 0.005–0.01 g once or twice a day

Maximal doses for adults single—0.025 g daily—0.05 g

Pain in the region of the intestine sometimes follows administration of the drug

Available in powder form and in tablets of 0.01 g

To be stored in well closed bottles in a dry place observing safety precautions (List B)

D Miscellaneous laxatives

MERCUROUS CHLORIDE CALOMEL (*Hydrargyrum chloratum mite Hydrargyri subchloridum Calomelas*) Hg₂Cl₂

Heavy white or slightly yellowish fine crystalline powder insoluble in water alcohol and ether slowly decomposes under the action of light

Used orally as a laxative and choleric also has a diuretic effect Adults are prescribed 0.1–0.5 g children from 0.02 to 0.05 g depending on their age Sometimes applied externally as an ointment in diseases of the cornea and in blennorrhoea as well as a prophylactic against venereal diseases

Maximal doses for adults single—0.5 g daily—1 g

Maximal doses for children 7–9 years old single—0.05 g daily—0.15 g 10–14 years single—0.05–0.075 g daily—0.15–0.2 g Children up to 7 years old are not prescribed mercurous chloride

Under the influence of bright light and moisture calomel may partially be converted into corrosive sublimate when prescribing calomel lactose is used as a nonhygroscopic ingredient Powders containing calomel must not be kept

long, especially in damp rooms Sodium chloride, iodine, acids and alkalis must not be prescribed simultaneously with calomel, acid or salty foods should be avoided

Calomel, being a mercury drug may have a toxic effect on the body and for that reason it is not used extensively today as a laxative, choleric or diuretic it is mainly used externally

To be stored in well closed bottles of amber glass in a place protected from light observing safety precautions (List B)

REST-HARROW (*Ononis arvensis*)

Perennial herb of the family Leguminosae which grows in the Caucasus Contains saponins and glycosides (ononin, onocerin, etc)

Used for normalizing the stool (loosening) chiefly in cases of hemorrhoid

Prescribed in the form of decoction or tincture (20% alcohol) The decoction is made by boiling 30 g of roots with 1 liter of water until 0.5 liter is left, and filtering off The decoction is taken 3 times a day before meals over a period of 2–4 weeks The tincture is taken in a dose of 1 teaspoonful, 2–3 times a day

FLUID EXTRACT OF FLAX WEED SEED (*Extractum Descurinae Sophiae fluidum*)

Fluid extract of the seeds of the Flax Weed (*Descurinia Sophia* (L.) Schur *Sisymbrium Sophia* L.), family Cruciferae, prepared with 70% alcohol

Transparent dark yellow liquid with pungent taste and characteristic odour Raises the tone of the intestinal muscles and intensifies contractions

Used as a laxative in functional atonic constipation

Prescribed orally 15–20 drops twice a day after meals for 3–5 days

To be kept in bottles of amber glass in a cool place

LAMINARIA (*Laminaria saccharina*)

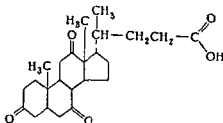
A brown seaweed of the family Laminariae grows profusely along the Far Eastern coast of the USSR and in the White and Black Seas Contains iodides and bromides alginates (calcium salts of alginic acids), mannitol the polysaccharide laminarin, vitamin C and other substances Used for medical purposes in the form of a powder — fine, dark grey scales with characteristic odour and salty taste

Chiefly used as a mild laxative in chronic atonic constipation The laxative effect is due to the fact that the preparation swells greatly and the increased volume irritates the receptors in the mucous membrane of the intestine Because of its iodide content Laminaria is indicated as a laxative in patients with symptoms of atherosclerosis

Prescribed in a dosage of $\frac{1}{2}$ –1 teaspoonful once a day When used for lengthy periods and if there is heightened sensitivity to iodine, symptoms of iodism are possible Not to be administered in nephritis, hemorrhagic diathesis and other conditions in which iodine containing drugs are contraindicated

VII CHOLERETICS

DEHYDROCHOLIC ACID



Synonyms *Acidum dehydrocholicum* Cholan DH Chologon Dehychol Dehydrocholin Didrocol Erebile Hykolex Ketocholamic acid Oxycholin Procholon

White crystalline powder odourless bitter taste almost insoluble in water soluble in alcohol Melting point 230—237°

Dehydrocholic acid belongs to the group of bile acids it is a physiological irritant of the liver cells stimulating the formation of bile Has a disinfecting effect in infections of the gall bladder and biliary tract Also acts as a diuretic

Used in cholangitis and chronic cholecystitis

Administered orally Dosage for adults 0.25—0.5 g 3 times a day Dosage for children up to 1 year old — 0.01—0.02 g 2—5 years — 0.03—0.1 g 6—12 years — 0.2—0.25 g

Available in tablets of 0.25 g

To be kept in well closed bottles of amber glass or in tubes in a cool dry place

SODIUM DECHOLATE (*Natrium decholicum*)

Synonyms Biliton Cholamin Decholin Dilabil sodium *Natrii dehydrocholas* Suprachol

Indications for use are the same as for chologon

Slowly injected intravenously once a day beginning with 5—10 ml 5% solution and gradually increasing the dose to 5—10 ml 20% solution Injections are given for 2—3 days followed by a break of 2—3 days

ALLOCHOL (*Allocholium*)

Tablets containing dry animal bile (0.08 g) dry garlic extract (0.04 g) dry nettle extract (0.005 g) and activated charcoal (0.025 g)

Used in chronic hepatitis cholangitis cholecystitis and habitual constipation Dose 2 tablets 3 times a day after meals

Available in vials containing 50 tablets

CHOLENZYM (*Cholenzymum*)

Preparation of bile and pancreatic and intestinal enzymes of slaughtered cattle

Used as a cholagogue in hepatitis cholecystitis and diseases of the gastrointestinal tract (gastritis achylia etc) Administered orally 1 dragee 1—3 times a day

Available in dragees of 0.5 g

To be stored in a cool dry place protected from light

CHOLOSAS

Extract of hips Thick dark brown liquid with characteristic odour and sweetish taste

Used in cholecystitis and hepatitis Administered orally adults — 1 teaspoonful 2—3 times a day children — $\frac{1}{4}$ — $\frac{1}{2}$ teaspoonful

Available in bottles containing 250 ml

EVERLASTING FLOWERS (*Flos Helichrysi arenarii*)

Dried not fully expanded flower heads of the wild Everlasting (*Helichrysum arenarium* L. or *Gnaphalium arenarium* L.) family Compositae Habitat sandy soils of the Ukraine the Crimea and the North Caucasus Active principles flavones bitter substances tannins sterines volatile oils and other substances

Used in the form of a decoction fluid extract or dry extract as a cholagogue in cholecystitis and hepatitis

Dry extract of Everlasting Flowers (*Extractum florum Helichrysis arenarii siccum*) Granulated powder containing a mixture of Everlasting extract and lactose (1 part of the preparation represents 4 parts of Everlasting Flowers)

Administered in a dose of 1 g 3 times a day Average length of treatment 2—3 weeks

Flamin (*Flaminum*) Dry Everlasting extract containing the total active principles of the plant Available in tablets of 0.05 g

Used in chronic cholecystitis and hepatocholecystitis 1 tablet 3 times a day half an hour before meals (to be taken with a small amount of warm water)
Course of treatment 10-14 days depending on the course of the disease

MAIZE SILK (*Stigmata Maydis Styli et stigmata Maydis*)

Styles and stigmas of maize (*Zea Mays* L.) family Gramineae gathered when the ears are ripening

Contains cytosterol stigmasterol fatty oils volatile oil saponin bitter glycosides vitamin C, vitamin K gum like substances etc

Used as a choleric and diuretic When maize silk preparations are taken orally the secretion of bile increases and its viscosity specific gravity and bilirubin content are reduced the content of prothrombin in the blood increases and the clotting time is shortened

Principal indications for use cholecystitis cholangitis and hepatitis with limited secretion of bile Can also be used on a par with vitamin K preparations as a hemostatic (principally in hypoprothrombinemia)

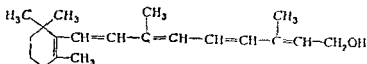
Administered in the form of an infusion (10 g per 200 ml), decoction or fluid extract The decoction is prepared by pouring 1½ glasses of cold water over 10 g of maize silk boiling 30 minutes over a small flame in a covered enamelled vessel cooling and straining 1-3 tablespoonfuls are taken every 3-4 hours

Chapter VIII

AGENTS CHIEFLY INFLUENCING THE PROCESSES OF TISSUE METABOLISM

I. VITAMINS

VITAMIN A (Vitaminum A) Axerophthol, Retinol



Synonyms Adatone Afaxin, Afilina Alfaergin Alphasterol Amulvit Amunine, Aphalin, Arovit, Asteril, Aterapion, Avimin Avital Avitan, Avitol, Axerol, Davitamon A, Euvit A Gadol, Oleovit A Prepalin Viadenin Vitadral, Vitalfa, Vitama, Vitaplex A Vitapur A Vogan, Xerophtol

Vitamin A is contained in animal fats butter, milk, cheese, egg yolk and caviar The main source for obtaining vitamin A preparations is the oil from the liver of marine animals (whale, walrus and seal) and some species of fish (cod sea perch, etc) Medicinal fish liver oil is prepared from these oils

Vitamin A itself is not found in vegetable foodstuffs, but many vegetables (carrot, spinach parsley, green onions, sorrel), red pepper and fruits (black currant, whortleberry, gooseberry, peach, apricot, etc) contain carotene, which is provitamin A

Vitamin A is formed in the body from carotene by means of an enzyme secreted by the liver

Vitamin A has now been synthesized In the pure form vitamin A crystallizes in pale yellow needles, melting point 63–64°, insoluble in water, soluble in alcohol and other organic solvents Decomposes under the action of light and air

Both vitamin A preparations of natural origin and synthetic vitamin A (acetate) are being used today in medical practice

Vitamin A is of great importance for the nutrition of man and animals and for preserving their health it promotes normal metabolism and the growth and development of the organism, ensures the normal activity of the organ of vision, has a favourable influence on the function of the tear, sweat and sebaceous glands heightens resistance to diseases of the mucous membranes of the respiratory passages and intestine, and increases the body's resistance to infection in general Because of these biological properties vitamin A is called

the antixerophthalmic and antimetabolic vitamin or the vitamin which defends the epithelium

In vitamin A deficiency (hypovitaminosis and avitaminosis) it is the organ of vision that is affected first of all the synthesis and decomposition of visual purple in the retina are upset adaptation to darkness is impaired and nocturnal blindness develops

If vitamin A deficiency is not eliminated in the initial stage of the disease more serious changes in the organ of vision may appear the conjunctiva and then the cornea become dry and dull (xerophthalmia and keratomalacia)

The deficiency of vitamin A in the body also causes metaplasia of the epithelial tissues and lowers resistance to infection the appetite deteriorates the weight declines fatiguability increases and the body becomes easily susceptible to infectious diseases There is often an onset of diseases of the digestive tract and respiratory passages particularly in children

The amount of vitamin A required varies depending on the physical work performed as well as on meteorological and climatic conditions (cooling excessive humidity overheating)

The dose of vitamin A should be raised for persons whose eyesight must meet special requirements because of their occupation (drivers engaged in transport fliers etc) There is also a greater need for vitamin A during pregnancy and lactation

The minimal daily vitamin A requirement ("hygienic dose") for adults and children is 3300 I U (International Units) which corresponds to 1 mg of pure vitamin

Optimal doses for adult performing the average amount of physical work—15 mg (5000 I U) for adults engaged in heavy labour—25 mg (8250 I U) for adults engaged in extremely heavy labour—3 mg (10 000 I U) for pregnant women—25 mg (8250 I U) for nursing mothers—3 mg (10 000 I U) for children up to 7 years old—15 mg (5000 I U) from 7 to 14 years—2 mg (6600 I U) over 14 years—25 mg (8250 I U)

Therapeutic daily doses in nyctalopia—10 000—25 000 I U in xerophthalmia—50 000—100 000 I U in skin symptoms—100 000 I U Children are prescribed divided doses of 5000—10 000 I U for therapeutic purposes up to 20 000 I U daily Large doses of vitamin A (50 000—100 000 I U daily) along with riboflavin are also recommended in retinitis pigmentosa

Vitamin A is widely used in some skin diseases especially in cases in which there is A hypovitaminosis and in which the process of keratinization is predominant (keratosis follicularis keratosis palmaris et plantaris etc), as well as in seborrheic eczema parapsoriasis etc In treating these diseases vitamin A is given in relatively large doses (100 000 I U a day) over a lengthy period

Maximal doses for adults single 50 000 I U daily—100 000 I U

Oil solutions of vitamin A are also used topically for the treatment of burns ulcers and frostbite After cleaning the affected area is painted with a solution of vitamin A and covered with gauze Vitamin A is applied up to 5—6 times a day as excoriation and epithelization progress the number of applications is reduced to one a day Simultaneously with external use up to 100 000 I U of vitamin A is given orally

The administration of vitamin A especially in large doses should be carried out under a physician's observation Side effects are possible when large doses are given over a lengthy period (symptoms of hypervitaminosis) diarrhoea loss of appetite hyperesthesia exophthalmia etc Hypoprothrombinemia may develop and ascorbic acid metabolism may be impaired

Vitamin A is administered in the form of fish liver oil preparations and synthetic vitamin A (acetate) as well as dragees and oil solutions Carotene and carotene preparations formerly used (caroton carotol vitaderm) are no longer being put out for medical purposes because of their low effectiveness

Oil solutions of vitamin A are available with a content of 100 000 I U 200 000 I U or 300 000 I U per ml The solution with a vitamin A content of 100 000 I U per ml can be dispensed for individual use

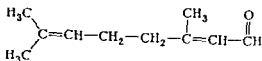
Solutions with a larger vitamin content are used for the vitaminization of foodstuffs (during their manufacture)

Vitamin A dragées are available with a content of 1 mg (3300 I U), 2 mg (6600 I U) or 3 mg (9900 I U)

Vitamin A is also an ingredient of compound (multivitamin) dragees Composition 0.5 mg (1650 I U) vitamin A, 1 mg vitamin B₁ (thiamine hydrobromide), 1 mg vitamin B₂ (riboflavin), 5 mg vitamin PP (nicotinic acid or nicotinamide), 25 mg vitamin C (ascorbic acid)

CITRAL (Citalum)

Similar in chemical structure to the side chain of the vitamin A molecule

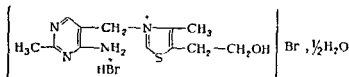


Yellowish oily liquid, insoluble in water characteristic lemon odour

Used in ocular practice in keratitis and conjunctivitis in the form of water alcohol solution (1:10,000), 1–2 drops are instilled into the conjunctival sac Has an analgesic and antiphlogistic effect Has also been proposed for oral administration in hypertensive disease, 10–20 drops of 1% alcoholic solution, 2–3 times a day

VITAMIN B₁; Thiamine Hydrobromide or Thiamine Hydrochloride (Vitaminum B₁, Thiaminum bromatum, Thiamini hydrobromidum, Thiaminum chloratum, Thiamini hydrochloridum)

N (2 methyl-4 amino 5 methylpyrimidyl) 4 methyl 5 β hydroxy ethylthiazolum bromide hydrobromide or chloride hydrochloride



Thiamine hydrobromide

Synonyms Aneurine Anevryl, Arcavit B₁, Bemunine, Benerva, Beneurin Benol, Berin, Belabion, Betalin, Betaneurin, Betavel Betavitan Betavin, Bethiamin, Bethiazine, Bevumin, Bevitall Bevitline Crystovibex, Oryzamin, Thiamine bromide (or chloride) Vitaplex B₁, Vitapur B₁

White crystalline powder with slight yellow tint, characteristic yeast odour, freely soluble in water and methanol, insoluble in ether Aqueous solutions are acid Melting point of hydrobromide 210–215°, melting point of hydrochloride 246–250° Decomposes rapidly in alkaline and neutral solutions stable in acid solutions Solutions are sterilized by holding at 100° for 30 min

Synthetic thiamine hydrobromide (or hydrochloride) fully corresponds to natural vitamin B₁

Vitamin B₁ occurs naturally in yeast and the germs and hulls of cereals, as well as in bread made with unbolled flour In white bread, which is freed of bran and germs, the vitamin B₁ content is sharply lowered In natural products vitamin B₁ is found both in the free and combined form, in the latter case it is phosphorized and combined with a protein carrier, thus being a co enzyme of carboxylase

The human body, like that of most animals, is incapable of synthesizing vitamin B₁, and ingests it with the food Surplus amounts are to some extent stored in the liver but the body cannot do without a supply of the vitamin from without for a lengthy period of time In the animal organism the greatest amount

of vitamin B₁ is in the liver and kidneys but the content in animal tissues is insignificant as compared with that in cereals. In spite of the fact that vitamin B₁ is present in most foodstuffs, the body's requirements are not always fully satisfied.

Vitamin B₁ plays an important part in vital activities. Since it is a constituent of co-carboxylase it is especially concerned in carbohydrate metabolism. Vitamin B₁ deficiency may lead to the accumulation of lactic and pyruvic acids in the tissues; this in turn may cause polyneuritis and impairment of cardiac activity. Ingestion of large amounts of carbohydrates with the food or for therapeutic purposes increases the vitamin B₁ requirement. Vitamin B₁ is of particular importance for the function of the nervous system and the digestive apparatus and for cardiac activity as well as for the endocrine system. It is also concerned in the regulation of the water exchange. It has been reported that vitamin B₁ is connected with the hemogenic organs.

The absence or lowered content of vitamin B₁ leads to an impairment of the body's functional activities and to the onset of a number of diseases primarily diseases of the nervous system.

The complete absence of vitamin B₁ in the food leads to the development of a serious form of avitaminosis — the disease beriberi.

B₁ hypovitaminosis is often observed parallel with B₁ avitaminosis; this may result from a protracted carbohydrate diet, the omission of rye bread from the ration, the feeding of patients for lengthy periods with food lacking in variety and deficient in vitamin B₁, etc. B₁ hypovitaminosis is characterized by a general loss of strength, low temperature, lassitude, edema and gastrointestinal disorders. Besides this, secondary avitaminosis and hypovitaminosis are also encountered; these result from an impairment of the absorptive ability of the gastrointestinal tract in various diseases (malignant neoplasms, ulcers, inflammatory processes, etc.).

Minimal daily requirement of vitamin B₁: children up to 7 years old — 1 mg; 7—14 years — 1.5 mg; adults performing an average amount of physical work — 2 mg; adults engaged in heavy physical labour, and pregnant women (from the 5th month) — 2.5 mg; adults engaged in extremely heavy physical labour and nursing mothers (up to the 7th month of lactation) — 3 mg.

Vitamin B₁ is employed as a specific therapeutic agent in B₁ avitaminosis and hypovitaminosis.

Besides its use for a prophylactic and therapeutic effect in the corresponding hypo- and avitaminosis, vitamin B₁ is administered in the presence of the following indications: neuritis (including lead, mercury, arsenic and other toxic polyneuritis as well as alcoholic polyneuritis), neuralgia, peripheral paralysis. Vitamin B₁ is also used in encephalopathy. Favourable results have been recorded in ulcer of the stomach and duodenum and gastrointestinal hypotonia as well as in diseases of the liver. Vitamin B₁ has been reported to have a favourable influence on coronary circulation; there being an abatement or disappearance of pain in patients with stenocardia and myocardial infarction, it has likewise been reported that vitamin B₁ is effective in spasms of the peripheral vessels (endarteritis, etc.).

In dermatological practice vitamin B₁ is used in dermatoses of neurogenic origin: pruritus of diverse etiology (icteric, diabetic, uremic, senile), pyoderma, tosis, eczema and psoriasis.

When analyzing the mode of action of vitamin B₁, it must be remembered that vitamin B₁ and other vitamins are more than specific "anti-avitaminosis" agents. By their active influence on various functions of the body and their intervention in metabolism and neuroreflex regulation they can have a favourable effect in various pathological processes and should therefore be looked on as pharmacotherapeutic substances in a broad sense.

Among the pharmacological properties of vitamin B₁, which are not directly connected with its vitamin properties and which merit attention is its power of influencing the transmission of neural impulses in the synapses. Like other com-

pounds containing a quaternary nitrogen atom (see p 123) it has ganglion blocking and curarelike properties, although manifested in moderate degree. By influencing polarization processes in the region of the neuromuscular synapses it can weaken the curarelike effect of some muscular relaxants (ditilin and others).

It may be that the effectiveness of vitamin B₁ in vascular spasm, pruritus and other pathological processes is partially due to its influence on the ganglia and other elements of neuroreflex regulation.

The therapeutic dosage of thiamine hydrobromide for adults with initial manifestations of B₁ hypovitaminosis is 0.006–0.012 g (6–12 mg) daily for 30 days. When there are changes in the nervous system, gastrointestinal tract or other systems, 0.012–0.018 g is administered orally 1–5 times a day, parenterally, usually intramuscularly (less often intravenously or subcutaneously), 0.012–0.06 g is administered daily for a course of 10, 20 or 30 injections.

Injections are usually given once a day. It should be borne in mind that vitamin B₁ is readily absorbed from the gastrointestinal tract and that the necessary concentration in the blood can be achieved by oral administration.

Subcutaneous injections of vitamin B₁ are painful because of the low pH of solutions. When administered intravenously and in high concentrations anaphylactic symptoms may be observed.

Children are prescribed thiamine hydrobromide in a dosage of 0.0024–0.006 g (2.4–6 mg) orally 1–5 times a day, or 0.006–0.012 g (6–12 mg) parenterally once a day.

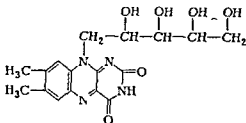
Available in dragees or tablets containing 12, 24, 6 and 12 mg and in ampoules containing 1 ml of 12, 24 and 6% solution.

Thiamine Hydrochloride. Thiamine hydrochloride C₁₂H₁₇ON₄SCl₂ (molecular weight 337.27) can be used instead of the hydrobromide (molecular weight 435.2), reducing the dose accordingly (0.005 g of the hydrochloride is used instead of 0.006 g of the hydrobromide, and so on).

Available in dragees or tablets containing 1, 2, 5 and 10 mg, and in ampoules containing 1 ml of 1, 2 and 5% solution.

To be stored in a dry place protected from light.

VITAMIN B₂, RIBOFLAVIN (Vitaminum B₂, Riboflavinum)



Synonyms: Belfavin, Belfavit, Belavitam, Flavaxin, Flavitol, Lactobene, Lactoflavin, Ovolflavin, Ribovin, Vitaflavine, Vitaplex B₂, Vitapur B₂.

Yellow-orange crystalline powder, odourless, bitter taste, sparingly soluble in water and alcohol. Aqueous solutions are yellow, showing an intense yellowish-green fluorescence. Unstable when exposed to light. Melting point 280° (with decomposition).

Vitamin B₂ is widespread in the plant and animal kingdom. In man it is ingested for the most part with meat and milk products. Contained in yeast, whey, egg albumin, meat, fish liver, peas, and cereal germs and hulls. Also produced synthetically.

When riboflavin enters the body it is phosphorylated and converted into riboflavinphosphate and flavin adenine nucleotide. Combined with protein it is a

component of the enzymes that regulate oxidation reduction processes Vitamin B₂ is involved in processes of carbohydrate protein and fat metabolism It plays an important part in maintaining the normal visual function of the eye

In man the deficiency or absence of vitamin B₂ in the food causes hyporiboflavinosis and then ariboflavinosis In hyporiboflavinosis deterioration of the appetite is observed along with loss of weight weakness headache a burning sensation in the skin pain in the eyes night blindness and tenderness in the lower lip and the corners of the mouth As the disease develops ulcers appear in the corners of the mouth (so called angular stomatitis), and a reddening of the mucosa of the mouth and tongue and seborrheic eczema of the face and ears are observed At the same time keratinization of the excretory ducts of the skin glands on the face and blepharitis are to be noted Ariboflavinosis may cause the development of conjunctivitis pericorneal congestion and clouding of the cornea and lens

Vitamin B₂ is used for therapeutic purposes in ariboflavinosis nyctalopia conjunctivitis iritis keratitis corneal ulcers cataract slow healing wounds and ulcers general malnutrition radiation sickness asthenia derangement of the intestinal function sprue Boikin's disease and other diseases

The daily requirement of vitamin B₂ for adults and children is 2 mg The therapeutic dosage in subacute ariboflavinosis 0.005—0.01 g (5—10 mg) daily for 10—15 days in more serious cases — 0.01 g 3—5 times a day for 1—1½ months Prescribed by mouth and at times topically in the form of eye drops

Available in dragees or tablets of 0.001 0.002 0.005 and 0.01 g

To be kept in tightly closed bottles of amber glass

NICOTINIC ACID (Acidum nicotinum)

Pyridine β carboxylic acid



Nicotinic acid



Nicotinamide

Synonyms Apelagrin Niacin Nicodan Nicodon Niconacid Nicotene Nicovit Pellagramin Pelonin Peviton Vitaplex N

White crystalline powder sparingly soluble in cold water (1 : 70) more so soluble in hot water (1 : 15) sparingly soluble in alcohol very slightly soluble in ether Melting point 234—237° Solutions are sterilized by holding at 100° for 30 min

Nicotinic acid and nicotinic acid amide (Nicotinamide Nicotinamidum synonym Niacinamide) are specific anti pellagra agents both are regarded as vitamin PP which is included in the vitamin B complex

Nicotinic acid and nicotinamide are contained in animal organs (liver kidneys muscles etc) milk yeast fruits and vegetables

Nicotinic acid and its amide play an important role in the body's vital activities they are prosthetic groups of the enzymes coenzyme I (diphosphopyridine nucleotide) and coenzyme II (triphosphopyridine nucleotide)

The administration of nicotinic acid has a favourable influence on all manifestations of pellagra changes in the central nervous system and gastrointestinal and skin symptoms The therapeutic significance of nicotinic acid is not limited to its antipellagra properties it also has a favourable effect in diseases of the liver and heart in ulcer of the stomach and duodenum and enterocolitis in slow healing ulcers and wounds

The detoxifying effect of nicotinic acid is of great practical importance The drug also acts as a vasodilator

Used in pellagra, diseases of the liver (acute and chronic hepatitis, cirrhosis), vascular spasms (spasms of the vessels of the extremities, kidneys and brain), non healing wounds and ulcers, infectious diseases (dysentery, typhoid, typhus, etc), and other diseases

Minimal daily requirement of nicotinic acid for children and adults — 15 mg; for pregnant women — 20 mg, for nursing mothers — 25 mg

For therapeutic purposes nicotinic acid is administered orally and parenterally. In pellagra, adults are given 0.1 g orally 2—4 times a day for 15—20 days, intramuscularly the dose is 0.1 g once or twice a day for 10—15 days, intravenously the dose is 0.05 g. Children are prescribed from 0.005 to 0.05 g 2—3 times a day.

In other diseases adults are prescribed 0.02—0.05 g 2—4 times a day, children — 0.005—0.02 g. Intravenous injections are given slowly. Subcutaneous and intramuscular injections of nicotinic acid are painful. In order to avoid irritation sodium nicotinate (the sodium salt of nicotinic acid) or nicotinamide can be used.

Maximal doses for adults orally single — 0.1 g, daily — 0.2 g (in pellagra — 0.5 g), intravenously, single — 0.05 g (in pellagra — 0.1 g), daily — 0.1 g (in pellagra — 0.3 g).

Maximal doses for children up to 6 months old, single — 0.005 g, daily — 0.015 g, from 6 months to 1 year, single — 0.008 g, daily — 0.024 g, 2 years, single — 0.01 g, daily — 0.03 g, 3—4 years, single — 0.015 g, daily — 0.045 g, 5—6 years, single — 0.025 g, daily — 0.075 g, 7—9 years, single — 0.03 g, daily — 0.09 g, 10—14 years, single — 0.05 g, daily — 0.15 g.

Side effects may be observed when nicotinic acid is used: reddening of the face and upper half of the trunk, vertigo, a sensation of rush of blood to the head, tickling in the fingers, urticaria. These symptoms pass away of themselves. When solutions of nicotinic acid are rapidly injected intravenously there may be a marked lowering of the arterial pressure.

Nicotinamide is administered in the same doses as nicotinic acid, it is tolerated better and does not cause reddening of the face or a feeling of rush of blood to the head, etc.

Nicotinic acid is available in powder form, in dragees or tablets of 0.005, 0.01, 0.025 and 0.05 g, and in ampoules containing 1 or 2 ml of 1, 2.5 and 5% solution.

To be stored in well closed bottles in a dry place, observing safety precautions (List B).

Calendula nicotinic acid tablets (CN tablets) Contain 0.25 g powdered flower heads of Calendula (*Calendula officinalis* L.) and 0.1 g nicotinic acid.

The findings of therapeutic institutions show that tablets of this composition reduce dyspeptic symptoms and intoxication, and improve the subjective feeling in patients with neoformations of the gastrointestinal tract. They have been proposed as a symptomatic agent having no specific therapeutic effect, for patients with neoformations of the oesophagus, stomach and intestine.

Patients are given $\frac{1}{4}$ — $\frac{1}{2}$ tablet the first few days, if this is tolerated well the dose is increased to $\frac{1}{2}$ —1 tablet twice a day.

The tablets are taken 10—15 min before meals, first crumbling them and mixing with water. Course of treatment 2—3 months, with a 3 day break after each 10 days of administration.

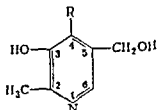
If there is a marked vascular reaction or other side effects the dose is reduced.

Tablets are to be stored in a cool dry place, observing safety precautions (List B).

VITAMIN B₆; Pyridoxine (*Vitaminum B₆*, *Pyridoxinum*, *Pyridoxini hydrochloridum*)

Synonyms Adermin, Beadox, Becilan, Bedoxin, Benadon, Besatin, Hexabitalin, Hexabion, Hexavibex, Pyrritol, Vitapur B₆.

Vitamin B₆ activity is possessed by a number of pyridine derivatives grouped together under the general term "pyridoxine", and differing from one another in the substituting groups at position 4



The compound in which $R=CH_2OH$ (2 methyl 3 hydroxy 4,5 pyridinedimethanol) is called pyrodoxol when $R=CHO$ the compound is known as pyridoxal and when $R=CH_2NH_2$ pyridoxamine.

2 methyl 3 hydroxy-4,5 pyridinedimethanol is put out for medical use in the form of the hydrochloride under the name of pyridoxine hydrochloride white crystalline substance of bitter taste freely soluble in water and alcohol. Melting point $204-206^\circ$. Aqueous solutions have a pH of 2.5-3.5, they decompose under the influence of light. Solutions are sterilized by holding at 100° for 30 min.

Vitamin B₆ is contained in plants and in animal organs, especially whole grains potatoes vegetables meat fish milk and ox liver. There is relatively little vitamin B₆ in yeast. The need for vitamin B₆ is satisfied by foodstuffs, it is also synthesized to some extent by the intestinal microflora.

Pyridoxine plays an important part in metabolism. On entering the body it is phosphorylated and converted into phosphopyridoxal, becoming a constituent of the enzymes which produce reamination of amino acids. Pyridoxine accelerates the metabolism of tryptophan, methionine, cysteine, glutamic acid and other amino acids.

Pyridoxine is also involved in fat metabolism.

Symptoms of B₆ hypovitaminosis may develop if insufficient pyridoxine is ingested with the food. In animals characteristic dermatosis (acrodynia), edema degenerative changes in the nervous system, epileptoid attacks and other derangements are observed. Prolonged vitamin B₆ deficiency fosters the development of fatty infiltration of the liver, and hypochromic anemia.

The changes which take place in the human body when there is a deficiency of vitamin B₆ have not been investigated sufficiently.

The average daily requirement of vitamin B₆ is 3 mg for an adult, 1 mg for children up to 1 year old and 2 mg for children from 1 to 10 years. The requirement increases during pregnancy.

Vitamin B₆ is now used for therapeutic purposes in various diseases: toxicosis of pregnancy, postencephalitic parkinsonism and other forms of parkinsonism, chorea, pellagra (in conjunction with nicotinic acid). It has been reported that pyridoxine is effective in radiation sickness, and in preventing or abating toxic manifestations (particularly polyneuritis) observed when administering isoniazid and similar antituberculosis drugs, and that it is likewise effective in Botkin's disease, hypochromic anemia, benzene poisoning, etc.

Pyridoxine is used in the skin diseases: clinic in seborrheic and non seborrheic dermatitis, herpes zoster, neurodermatitis, psoriasis, exudative diathesis and other diseases.

Findings have been published on the lowering of the cholesterol content in the blood of patients with atherosclerosis under the influence of pyridoxine, and on the possible importance of this vitamin in the prevention and cure of atherosclerosis.

Pyridoxine is administered by mouth, intramuscularly or subcutaneously. The usual daily dose (orally or parenterally) is 0.05-0.1 g (in one or two administrations). The course of treatment ranges from one to three months, depending on the condition.

ding on the severity of the disease and the effectiveness of treatment In toxicosis of pregnancy it is advisable simultaneously to prescribe vitamins B₁ and B₂ and nicotinic and ascorbic acid When symptoms of toxicosis disappear the daily dose is reduced to 0.005–0.01 g

When using isoniazid phthivazid and other derivatives of isonicotinic acid hydrazide it is advisable to prescribe 0.05 g pyridoxine daily to prevent neuritis and other complications

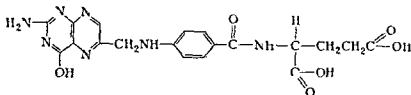
In peripheral neuritis pyridoxine is prescribed in a dose of 0.1 g daily in postencephalitic parkinsonism 0.1 g pyridoxine is administered daily for 1–3 months

Available in tablets of 0.005 and 0.01 g and in ampoules containing 1 ml of 1:2.5:5 and 10% solution

To be stored in a place protected from light

FOLIC ACID (Acidum folicum)

Pteroglutamic acid N [4 [(2-amino-4-hydroxy-6-pteridyl) methyl] amino] benzoyl] glutamic acid



Synonyms Vitamin B₉ Cytfol Folacid Folacin Folamin Folcidin Foline Folicil Folsan Folvite Pfolin

Yellow fine crystalline powder sparingly soluble in water insoluble in alcohol ether and other organic solvents soluble in solutions of alkalis and in concentrated mineral and organic acids Aqueous solutions are unstable on exposure to light

Contained in fresh vegetables (string beans spinach tomatoes carrots cauliflower etc) the leaves of plants are a particularly rich source and it is likewise found in the liver and kidneys of animals It is also produced synthetically

Folic acid is a constituent of the vitamin B complex It consists of a pteridine nucleus and glutamic and para-aminobenzoic acids (see p. 197) It is active in blood production along with vitamin B₁₂ it stimulates erythropoiesis It is also involved in the synthesis of amino acids (methionine serine etc) and in choline metabolism (by promoting the liberation of methyl groups)

Folic acid is used to intensify erythropoiesis in macrocytic anemia and sprue It is only slightly effective in aplastic anemia In pernicious anemia it is used in conjunction with vitamin B₁₂ or liver preparations folic acid alone is less effective and has no influence on changes in the nervous system (funicular myelosis) In sprue folic acid abates or eliminates the clinical manifestations of the disease and normalizes blood formation in this disease it is advisable simultaneously to prescribe liver preparations and hemotherapy Folic acid is also used in anemia caused by the administration of medicines Because of the favourable influence folic acid has on the function of the intestine its use is recommended in chronic gastroenteritis and tuberculosis of the intestine

The daily requirement of folic acid is 2 mg for an adult 0.5 mg for children up to 1 year old and 1 mg for children from 1 to 10 years For therapeutic purposes folic acid is prescribed orally or intramuscularly 0.01–0.03 g 1–3 times a day for 20–30 days

Available in tablets of 0.001 and 0.002 g

To be stored in well stoppered vials of amber glass, wrapped in black paper

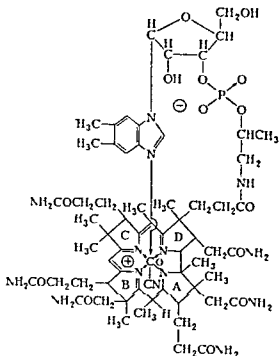
VITAMIN B₁₂ Cyanocobalamin (Vitaminum B₁₂ Cyanocobalaminum)

Synonyms Anacoblol Bedumil, Bchepan, Bendogen Beniform Berubigen, Biopar, Cobastab, Cobione, Cycobemin, Cycoplex Cytacox, Cytamen, Cytobex, Cytobion Distilvit Dobelin Docemine, Docilon Dodecavit, Heparitone, Reda min Rubavit Rubivital, Rubramin Systobex Vibicon

Vitamin B₁₂ has a complicated structure a peculiarity of its molecule is the presence of a cobalt atom and a cyano group which form a coordination complex

In the pure form vitamin B₁₂ occurs as dark red needles colourless and odourless dissolves in water forming red or pink solutions Decomposes without melting at 300—320° Aqueous solutions are sterilized by holding at 100° for 30 min or at 120° for 15 min, the vitamin decomposes if autoclaved for longer periods Oxidizing or reducing substances (e.g. ascorbic acid) and the salts of heavy metals foster the inactivation of the vitamin Microflora quickly ingests vitamin B₁₂ and solutions should therefore be kept in aseptic conditions

Vitamin B₁₂ is not formed by animal tissues it is synthesized in nature by microorganisms chiefly bacteria actinomyces and blue green algae Synthesized in the human and animal body by the microflora of the intestine from whence it enters the organs being accumulated in the greatest amounts in the kidneys liver and intestinal walls The amount of vitamin B₁₂ required by a person, i.e. the "hygienic dose" (0.00001—0.00002 g or 10—20 µg¹) is not fully ensured by synthesis in the intestine additional amounts are ingested with foodstuffs of animal origin Vitamin B₁₂ is contained in various amounts in medicinal preparations obtained from the livers of animals (see Campolon and Anti anemin)



¹ microgram (µg) = 0.000001 g = 1 γ (gamma)

Vitamin B₁₂ is the most active of modern antianemic agents. The mode of action has not been elucidated sufficiently but it has been established that vitamin B₁₂ is involved in the synthesis of labile methyl groups and in the formation of choline, methionine, creatine and nucleic acids, it has an active influence on the accumulation in the erythrocytes of compounds containing sulphydryl groups, it is concerned in the metabolism of fats and carbohydrates, and has a favourable influence on the function of the liver and the nervous system.

Vitamin B₁₂ has a pronounced therapeutic effect in Addison Biermer's disease, agastric anemia (after resection of the stomach), anemia associated with polyposis and syphilis of the stomach, anemia accompanied by enterocolitis, as well as other pernicious like anemias, including anemia due to invasion by the broad tapeworm and anemia in pregnancy, sprue, etc.

Doses of vitamin B₁₂ depend on the character and severity of the disease. In Addison Biermer's disease and other pernicious anemias the intramuscular administration of 30–50 µg once in 2–3 days has a marked hematological effect. A reticulocyte crisis usually sets in on the 4–6th day, after which the administration of 15–30 µg once or twice a week is sufficient to maintain the hematological remission. These doses, however, do not prevent the development of funicular myelosis and do not eliminate its symptoms. It is therefore necessary to administer vitamin B₁₂ in large doses in order to prevent or abort all manifestations of Addison Biermer's disease.

At present, in cases of uncomplicated pernicious anemia a dose of 50–100 µg (0.00005–0.0001 g) is administered once in 2–3 days. These doses usually cause a reticulocyte crisis on the 4–6th day with a subsequent increase in the amount of hemoglobin and in the number of erythrocytes, leukocytes and thrombocytes. Treatment with these doses is continued until clinical and hematological remission is achieved. A maintenance dose is then given — 100 µg once or twice a month.

In pernicious anemia with symptoms of funicular myelosis and in macrocytic anemia with affections of the nervous system 100–200 µg (0.1–0.2 mg) is given each second day for one month, or 5–10 injections of 500, 750 or 1000 µg (0.5, 0.75, 1 mg) are given, one injection in 2 days, and then 100–200 µg is administered each second day until the end of the month. Maintenance doses of 100 µg (0.1 mg) are given once or twice a month.

In other forms of anemia injections of 30–100 µg are given 2–3 times a week.

Treatment with vitamin B₁₂ should be combined when necessary with the prescription of other medicinal agents. In cases of a marked polyneuritic syndrome vitamin B₁ is administered simultaneously, in secretory insufficiency of the stomach (observed as a rule in Addison Biermer's disease) gastric juice or dilute hydrochloric acid is prescribed regularly. If the colour index should become hypochromic during treatment, and also in cases of hypochromic anemia, iron preparations are prescribed in addition (reduced iron or iron carbonate, 1 g 3 times a day after meals, simultaneously with 0.1–0.2 g ascorbic acid).

In pernicious coma transfusion of blood or erythrocyte mass is performed simultaneously with the administration of vitamin B₁₂.

Vitamin B₁₂ is also prescribed in macrocytic anemia in children, anemia resulting from poisoning with lead, benzene or drugs, radiation sickness, anemia and dystrophy in premature infants and in newly born infants following infections, sprue (in conjunction with folic acid), diseases of the liver (Botkin's disease, hepatitis, cirrhosis), polyneuritis, trigeminal neuralgia and diabetic neuritis, causalgia, migraine and alcoholic delirium, amyotrophic lateral sclerosis, infantile cerebral paralysis (Little's disease), skin diseases (psoriasis, photodermatosis, dermatosis herpetiformis, neurodermatitis, etc.).

In these diseases vitamin B₁₂ is used in doses of 100–1000 µg per injection. After improvement or the elimination of symptoms the dose is reduced.

In dystrophy in small children 15–30 µg is administered each second day.

Vitamin B₁₂ is usually administered parenterally intramuscularly or subcutaneously. Injections are painless and do not cause allergic reactions or toxic symptoms.

The endolumbar administration of vitamin B₁₂ has also been reported. The injection of 15–30 µg (up to 200 µg) of the vitamin into the spinal canal after the removal of 1–2 ml of spinal fluid once in 3–4 days proved effective in funicular myelosis and amyotrophic lateral sclerosis (L. I. Yivorkovsky and S. Y. Isakbaeva, A. V. Ordikhovsky).

Vitamin B₁₂ is poorly absorbed when taken by mouth. The presence of the so called intrinsic factor in the stomach is necessary for absorption and this is absent in patients with pernicious anemia. When prescribing vitamin B₁₂ orally it is necessary simultaneously to prescribe a special preparation of the mucous membrane of the pyloric part of animal stomach which contains Castle's intrinsic factor (gastr mucoprotein). Special tablets are prepared for oral administration containing vitamin B₁₂ and the intrinsic factor (mucovit).

Treatment with vitamin B₁₂ should be carried out under a physician's observation; the composition of the peripheral blood must be examined regularly. If there is a tendency toward the development of erythro- or leukocytosis the dose is lowered or treatment temporarily stopped.

In patients with stenocardia vitamin B₁₂ must be used with caution and in smaller doses (up to 100 µg per injection).

Available in powder form and in ampoules of 1 ml containing 0.00005 g (50 µg), 0.0001 g (100 µg), 0.0002 g (200 µg) or 0.0005 g (500 µg).

Liver extract. Concentrated water extract of ox liver or the liver of marine mammals (whale or dolphin). Transparent dark yellow liquid with odour of phenol (preservative).

Vitamin B₁₂ is one of the active principles of campolon, the content being up to 1.3 µg per ml. Campolon also contains other substances from liver tissue which increase its effectiveness.

Used in pernicious anemia and other forms of anemia and also in hepatic cirrhosis of the liver, atrophic gastritis and some forms of secondary anemia.

Administered intramuscularly: adults 2–4 ml daily or each second day, children up to 1 year — 0.5 ml, 2–5 years — up to 1 ml, 6–12 years — up to 2 ml. The course of treatment until a persistent remission is obtained is usually 25–40 days.

If the anemia acquires a hypochromic character, iron compounds are prescribed in addition.

In order to prevent relapses campolon is administered in a dosage of 2–4 ml twice a month. Injections are made less painful by mixing the campolon in the syringe with 1 ml of 1% procaine hydrochloride solution.

In pernicious coma "shock" doses of campolon (16–20 ml) are given simultaneously with the transfusion of blood or erythrocyte mass.

Intramuscular injections of campolon are often painful and there are sometimes allergic skin reactions.

Available in ampoules of 2 ml.

To be stored in a cool place protected from light.

Rp Campolon 20

D t d N 10 in amp

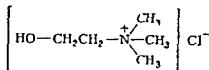
S 2 ml intramuscularly once a day

Antiflanemin (Antianaeminum). Water extract of ox liver to which 1.67 mg% cobalt sulphate has been added. The vitamin B₁₂ content is 0.6 µg per ml.

Indications for use are the same as for campolon. Administered intramuscularly: adults — 2–4 ml daily, children — 0.5–2 ml daily. In more severe cases the dose for adults is increased to 6–8 ml daily.

Available in ampoules of 2 ml.

CHOLINE CHLORIDE (*Cholinum chloratum*)
(2 Hydroxyethyl) trimethylammonium chloride



Synonyms *Bilineurine Cholinii chloridum Luridine*

White crystalline hygroscopic substance characteristic odour freely soluble in water pH of 10% solution=4.65

Choline belongs to the vitamin B complex. It is the initial substance from which acetylcholine one of the principal mediators of the neural impulse is formed in the body (see p. 87)

Choline forms part of the phospholipid lecithin which is an important constituent of the cells of the organism. It plays an important role in phospholipid metabolism and is involved in the synthesis of phospholipids in the liver. An insufficiency of choline in the animal organism leads to fatty infiltration and hemorrhagic degeneration of the liver and kidneys and involution of the thymus gland.

Choline is one of the most important so called lipotropic substances which prevent or diminish fatty infiltration of the liver. It is also an important source of methyl groups which are necessary for the biochemical processes taking place in the organism.

Choline has a slight acetylcholine effect; it somewhat stimulates the intestinal muscles. In large doses it can cause strong stimulation of the m. cholinoreactive systems.

Choline chloride is used in diseases of the liver: Botkin's disease, hepatitis and cirrhosis of the liver (mostly in the early stages).

It is administered by mouth or intravenously.

Orally it is taken in the form of a 20% solution 1 teaspoonful (5 ml) 3—5 times a day (3—5 g choline chloride per day).

Intravenously choline chloride is administered by the drip method in the form of a 1% solution in isotonic saline or in 5% glucose at a rate of not more than 30 drops per min. Up to 200—300 ml of solution is given in one infusion (2—3 g of choline chloride).

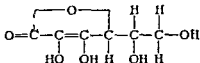
Intravenous infusions are augmented by the administration of a 20% solution orally.

The length of the course of treatment depends on the peculiarities of the case and ranges from 7—10 days up to 3—4 weeks or more; the total amount of the drug amounting to 80—100 g.

In rare cases dyspeptic symptoms are observed when choline chloride is taken orally. When rapidly administered intravenously a sensation of fever and nausea may be observed and at times vomiting, bradycardia and lowering of the arterial pressure collapse may develop. These symptoms are due to stimulation of the cholinoreactive systems. In order to avoid them choline chloride is administered intravenously only by the drip method. Treatment with choline chloride should be carried out on an inpatient basis.

Available in ampoules containing 10 ml 20% solution and in bottles containing 100 ml 20% solution. For drip infusions a 1% solution is prepared *ex tempore*.

VITAMIN C ASCORBIC ACID (*Vitaminum C Acidum ascorbinicum Acidum ascorbicum*)



Synonyms Ascorbin, Ascorbil, Ascorvit, Cantan, Cantaxin, Cebione, Cecon, Celin, Cenelon, Cevalin, Cevex, Larascorbine, Redoxon, Scorbumine, Vicin, Vitascorbol

Colourless crystals, acid taste, soluble in water (1:35), less soluble in alcohol (1:21) Melting point 189°.

Synthetic ascorbic acid fully corresponds to natural vitamin C. In nature, vitamin C is contained in considerable amounts in products of plant origin (hips, coniferous needles, cabbage, all leafy vegetables, lemons, oranges and other fruit, berries, horse radish etc.) Small amounts of vitamin C are found in animal products (liver, brain, muscles). Vitamin C is of great importance in the body's vital activities. Thanks to the presence of a dienol group ($-\text{COH}-\text{COH}-$) in its molecule it has marked reducing properties, it is involved in the regulation of oxidation-reduction processes, carbohydrate metabolism, capillary permeability and the coagulability of the blood and tissue regeneration. It is also involved in the formation of steroid hormones.

The human body is incapable of synthesizing vitamin C; the required vitamin C is ingested with the food. The deficiency or absence of the vitamin leads to the development of hypo- or avitaminosis (scurvy).

Daily requirement of vitamin C: adults performing average amount of physical work — 50 mg, adults engaged in hard physical labour — 75–100 mg, pregnant women — 75 mg, nursing mothers — 100 mg, children up to 7 years old — 30–35 mg, children over 7 years old — 50 mg.

Crystalline ascorbic acid and preparations containing it are used for prophylactic and therapeutic purposes in all cases when the body is in need of an additional amount of the vitamin. Ascorbic acid is given for the prevention and cure of scurvy. It is also administered in hemorrhagic diathesis (hemophilia, etc.), nosebleed and pulmonary, renal, uterine and other hemorrhages, hemorrhage caused by radiation sickness, as well as by overdosage of dicoumarol and other anticoagulants, infectious diseases and intoxications, Addison's disease, slow healing wounds and fractures, hypotrophy and other pathological processes. It is also prescribed in cases of heavy physical work or mental strain, and during pregnancy and lactation.

It has been reported that the use of ascorbic acid along with the proper hygienic regimen can prevent the development of atherosclerosis.

Ascorbic acid is administered orally (after meals), intramuscularly or intravenously. Therapeutic doses when administered orally: adults — 0.05–0.1 g, 3–5 times a day; children — 0.05–0.1 g, 2–3 times a day. Parenterally, adults are given 0.1–0.5 g daily, children — 0.05–0.2 g daily (in one or two injections). The length of treatment depends on the character and course of the disease.

Ascorbic acid is tolerated well. Contraindications for intravenous administration: heightened coagulability of the blood, thrombophlebitis and tendency toward thrombosis.

When using large doses of ascorbic acid for lengthy periods, it should be borne in mind that the vitamin may have a depressing influence on the function of the islands of Langerhans; consequently the functional ability of the pancreas must be regularly tested during treatment. Because of ascorbic acid's stimulating influence on the formation of cortisone, desoxycorticosterone and other steroid hormones, which under certain conditions may cause injury to the glomeruli of the kidneys and the development of a hypertensive reaction, the arterial pressure must be regularly checked during treatment with large doses of the vitamin (M. F. Merzhinsky and L. S. Cherkasova).

Available in powder form, in tablets or dragees containing 0.05 g, 0.1 g and 0.2 g; and in ampoules containing 1, 2 and 5 ml of 5 and 10% solution, or 1 ml 25% solution, as well as ampoules containing 10 or 20 ml 1% ascorbic acid solution in 40% glucose.

Ampoules are also available containing 1 ml of 5 or 10% solution of sodium ascorbate. Sodium ascorbate solutions have a pH of 4.4–6.2 and do not irritate

the tissues they can be injected subcutaneously, as well as intravenously and intramuscularly

Ascorbic acid is likewise a constituent of multivitamin tablets

Solutions of ascorbic acid are to be stored in sealed ampoules the powder is to be stored in small bottles of amber glass filled to the top, well closed and sealed with paraffin wax, and kept in a place protected from light

HIPS (*Fructus Rosae*, *Fructus Cynosbati*)

Dried ripe hips of various species of wild rose the Cinnamon Rose (*Rosa cinnamea* L.), the Needle Rose (*R. acicularis* Lindb.), the Daurian Rose (*R. dahurica* Pall.), Fedchenko's Rose (*R. Fedtschenkoana* Rgl.), etc Family Rosaceae

Contain vitamins C, K and P, sugar, organic acids, tannin and other substances The vitamin C content should be at least 1% in entire hips, and at least 18% in cleaned (cut) hips

Used in the form of infusions, extracts, syrups, pills, candies and dragees

An infusion of whole hips is prepared in the following way pour a glass of boiling water over 1 tablespoonful (20 g) of hips, boil 10 min in a covered enamelled vessel, let stand 22—24 hrs, and strain off The cleaned hips are boiled 10 min in a closed enamelled vessel, 20 g to 2 glasses of water, let stand 2—3 hrs, and strained off

The infusion is drunk in doses of $\frac{1}{4}$ — $\frac{1}{2}$ glass twice a day Children are given $\frac{1}{8}$ — $\frac{1}{4}$ glass To improve the taste, sugar, syrup or the like are added

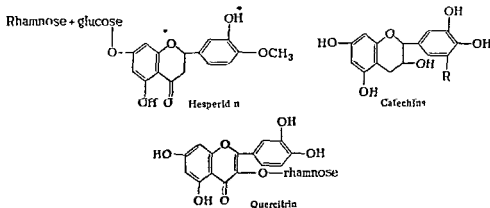
VITAMIN P (Vitaminum P)

A number of flavonoid substances belong to the vitamin P group they have the capacity of reducing the permeability and fragility of the capillaries, particularly in combination with ascorbic acid Along with ascorbic acid they take part in oxidation reduction processes in the body They also have the ability of inhibiting hyaluronidase Besides this they possess antioxidant properties, preventing, in particular, the oxidation of adrenalin

They are contained in the form of glycosides in many plants, especially in hips, lemons and other citrus fruits, unripe walnuts black currants, rowan berries and green tea leaves

The vitamin P activity of the following substances has been described, flavonones (hesperidin, eriodictin), flavonols (rutin, quercitrin, etc), chalcones (hesperidin methylchalcone), catechins (1 epicatechin, 1 epigallocatechin, etc), coumarins (esculin), gallic acid and other substances

The following preparations are of practical importance in medicine a) a catechin complex obtained from tea leaves and arbitrarily called "vitamin P"; b) rutin obtained from buckwheat (green mass) and from the flower buds of Japanese sophora Abroad, use is also made of hesperidin (from by products in making citrus juices), esculin (from the pericarps of the Horse Chestnut), and other preparations



Vitamin P from tea leaves is an amorphous yellow green powder of bitter astringent taste, soluble in water and alcohol

Used for the prevention and cure of P hypo and avitaminosis and in diseases accompanied by a derangement of the permeability of the capillaries hemorrhagic diathesis, retinal hemorrhage, capillarotoxicosis, radiation sickness, septic endocarditis, rheumatism, glomerulonephritis, hypertensive disease and arachnoiditis. Likewise used for the prevention and cure of capillary affections associated with the use of anticoagulants (dicoumarol and its analogues), salicylates and arsenous compounds

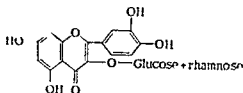
Administered orally. Dose for adults 0.05—0.1 g, 3—5 times a day. Dose for children 0.05 g 2—3 times a day. Vitamin C is given simultaneously with vitamin P in a dose of 0.2—0.5 g daily. The average course of treatment is 2—3 weeks. When necessary, the course is repeated after a break of 5 days.

In order to judge of the effectiveness of treatment it is recommended that the permeability of the capillaries should be examined by the Nesterov or Landis test or some other.

Contraindicated in patients with heightened coagulability of the blood.

Available in powder form and in dragees or tablets of 0.005, 0.01, 0.025 and 0.05 g as well as in tablets containing vitamin P (0.025 and 0.05 g) and vitamin C (0.05 and 0.1 g).

RUTIN (Rutinum)



Synonyms: Birutan, Eldrin, Farutine, Idorutin, Melin, Myrticolorin, Oxytin, Phytomelin, Rucetin, Rutabion, Rutosidum, Ruvit, Sclerutin, Violaquercitrin.

Contained in the leaves of Rue (*Ruta graveolens* L.) and other plants. Obtained for medical use from Buckwheat (green mass) and from the flower buds of *Sophora japonica*, family Leguminosae.

Yellow crystalline powder, odourless and tasteless, sparingly soluble in water.

Rutin is a vitamin of the P group. Indications for use are the same as for vitamin P from tea leaves.

Usually prescribed in daily doses of 0.06—0.15 g or more, but not in excess of doses indicated for vitamin P.

The dosage and length of treatment should be individualized depending on the clinical picture and the results of capillary permeability determinations. The average course of treatment is 5—6 weeks. It is recommended that ascorbic acid should be prescribed along with rutin. Contraindicated in cases of heightened coagulability of the blood.

Available in powder form and in tablets of 0.02 g as well as tablets containing 0.025 g rutin and 0.005 g ascorbic acid.

The following soluble rutin preparations have also been recommended: urutin (0.025 g rutin and 0.05 g methenamine in 1 ml distilled water) and rutamin (0.05 g rutin and 0.075 g procaine base in 1 ml water). Available in ampoules of 1 and 2 ml. Injected subcutaneously or intramuscularly, 1 ml once a day. Given in courses of 30—60 injections.

Rutin is to be kept in hermetically sealed bottles of amber glass in a place protected from light.

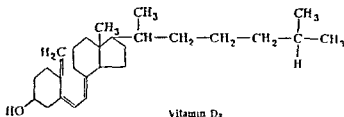
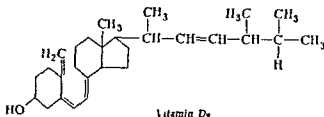
VITAMIN D (Vitaminum D) Antirachitic vitamin

Synonyms of vitamin D₂ Aldevit, Calciferolum, Deltalin, Detamin, Drisdol, Ergocalciferol, Fordetol, Infadin, Ostelin, Ultranol, Vigantol, Viosterol, Vitadol, Vitaplex D, Vitasterol

There are several forms of vitamin D (D₁, D₂, D₃, D₄, D₅)

Practical importance is today attached to vitamin D₂ (calciferol or ergocalciferol) and vitamin D₃ (cholecalciferol)

Vitamin D₂ is prepared by ultraviolet irradiation of ergosterol, a substance contained in yeast and vegetable oils. Vitamin D₃ is a product of the ultraviolet irradiation of 7 dehydrocholesterol (provitamin D), which is contained in the skin of man and animals. The two forms of the vitamin have equivalent biological activity.



In the pure form both vitamins are colourless crystalline substances insoluble in water, soluble in fats. Melting point vitamin D₂—115—117°, vitamin D₃—82—83°.

Vitamin D is contained in small amounts in egg yolk, caviar, butter and milk. Contained in large amounts (along with vitamin A) in the liver and fatty tissues of fish especially codfish, and also in the liver of the seal and other marine mammals.

Vitamin D regulates the metabolism of phosphorus and calcium in the body, it promotes the absorption of these substances by the intestine and their timely deposit in growing bone, it intensifies metabolism in the cells of the body and is a specific antirachitic agent.

Children who do not receive a sufficient amount of vitamin D with their food develop rickets. The milk of mothers receiving ordinary food does not contain vitamin D. It is only when copious supplies are introduced into the food or when nursing mothers are subjected to ultraviolet irradiation that the vitamin can be detected in the milk in perceptible amounts.

Before clinical manifestations of rickets develop, symptoms of D hypovitaminosis are observed — so called latent rickets which is accompanied by changes in metabolism, irritability, motor unrest, etc.

The potency of vitamin D preparations is expressed in international units (I U). 1 I U contains 0.000025 mg (0.025 µg) of the pure vitamin.

The minimal daily requirement of vitamin D is 1000 I U for adults, and 500—1000 I U for children.

Most of the vitamin D necessary for the human body is formed in the skin. If an insufficient amount of vitamin D is formed in the body, the deficit must be made up by taking preparations containing it.

For the prevention of rickets in children, vitamin D is prescribed in the following amounts during the entire autumn and winter seasons infants 1 month old—800—1000 I U infants beginning with 2nd—3rd month—2000—3000 I U For artificially fed children the daily dose of vitamin D is increased to 4000—10000 I U

Vitamin D is given simultaneously with fish liver oil which is prescribed for all children

For the treatment of rickets vitamin D is prescribed in a daily dosage of 10000—20000 I U in 2—3 administrations over a period of 1½—2 months Nursing mothers whose babies are suffering from rickets are prescribed 20000 I U of vitamin D daily

In acute rickets especially in premature infants large amounts of vitamin D are prescribed up to a total dose of 600000—800000 I U which is given in equal divided doses over a period of 3—6 days

The activity of vitamin D is increased when given simultaneously with salts of phosphorus and calcium (1 teaspoonful of 5—10% calcium chloride solution or 0.25 g calcium gluconate 2—3 times a day)

Vitamin D is also prescribed in cases of impaired function of the parathyroid glands in particular tetany and bone diseases due to abnormal calcium metabolism likewise prescribed in some forms of tuberculosis, psoriasis etc.

For the prevention of attacks of tetany up to 100000 I U of vitamin D daily is prescribed

Vitamin D is an effective agent for the treatment of all forms of lupus of the skin and mucous membranes The daily dose of vitamin D for adults suffering from tuberculous lupus is usually 100000 I U Children up to 16 years old suffering from tuberculous lupus are prescribed from 25000 to 75000 I U a day depending on the age The daily dose is given in two administrations during meals The course of treatment is 5—6 months

The maximal daily dose of vitamin D for adults is 100000 I U

Vitamin D is contraindicated in active forms of pulmonary tuberculosis diseases of the gastrointestinal tract ulcer of the stomach and duodenum acute and chronic diseases of the liver and kidneys and organic heart disease with a tendency toward decompensation

Side effects may develop when giving high doses of vitamin D loss of appetite nausea headache general weakness elevated temperature and the appearance of hyaline casts albumin and leukocytes in the urine In most cases these symptoms quickly pass away when a break is made in treatment or the dose reduced The toxic effect of large doses of vitamin D is lowered when vitamin A is given simultaneously

Caution must be observed when prescribing vitamin D for patients of advanced age—since the vitamin intensifies the depositing of calcium in the body it may foster the development of atherosclerosis It must also be remembered that vitamin D has a cumulative effect.

Vitamin D₂ is available in the following preparations

Oil solution—1 ml contains 10000 or 50000 I U

Alcoholic solution—1 ml contains 200000 I U

Dragees—each pill contains 300 or 500 I U

Fish liver oil also contains vitamin D Natural cod liver oil has a content of 30 I U per g vitaminized oil—150—250 I U

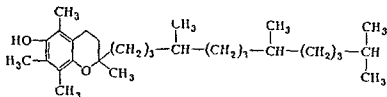
Vitamin D preparations including fish liver oil must be protected from light and air during storage to prevent inactivation the oxygen of the air oxidizes vitamin D while light converts it into poisonous toxisterol Safety precautions must be observed during storage of vitamin D and vitamin D preparations (List B)

VITAMIN E (Vitaminum E)

The name vitamin E is applied to a number of substances (tocopherols) which possess vitamin properties α tocopherol β tocopherol γ tocopherol δ tocopherol

They are widely present in plant products, especially wheat germ oil, and maize, ground nut, soya, sea buckthorn and other vegetable oils. Contained in insignificant amounts in animal products.

α Tocopherol is the most active.



α Tocopherol

The other tocopherols differ in the number and location of the methyl groups in the benzene nucleus.

The tocopherols are yellow, oil like substances insoluble in water, soluble in fats and organic solvents.

Vitamin E preparations are sold abroad under the following names: Ecofrol, Ephynal, Erevit, Tocomine, Tocopherex, Tocopherol, Tofavin, Tokophin, Viteo lin, etc.

Vitamin E is of all round significance for the organism of man and animals. In experimental animals not receiving vitamin E degenerative changes in the skeletal muscles and the myocardium are observed along with increased permeability and fragility of the capillaries, and degeneration of the epithelium of the seminiferous tubules. Hemorrhage is observed in embryos, and their intrauterine resolution gradually takes place. Degenerative changes in the nerve cells and affection of the parenchyma of the liver also occur.

Vitamin E is an active antioxidant. It inhibits carbohydrate metabolism in the tissues and protects various substances from oxidation changes, it likewise inhibits the metabolism of proteins, nucleic acids and steroids.

Vitamin E is used in muscular dystrophy, amyotrophic lateral sclerosis and other nervous diseases. It has been reported that vitamin E is effective in inflammatory and degenerative changes in the retina (reduction of edema, intensification of circulation, improvement of the visual function), psoriasis and skin ulcers, and lupus erythematosus.

Findings on the effectiveness of vitamin E for the prevention of habitual abortion and for the treatment of primary and secondary amenorrhea and sterility, as well as in coronary insufficiency are contradictory.

Available in oil extracts containing from 0.3 to 2% α tocopherol (to be taken in a dose of 1 teaspoonful daily), dragees or capsules containing 0.025, 0.05, 0.1 and 0.2 g of synthetic α tocopherol acetate in solution, ampoules containing 0.05, 0.1 and 0.2 g α tocopherol acetate in 1 ml oil solution.

Vitamin E is to be kept in well closed containers in a cool, dry place, protected from light. Ultraviolet rays destroy the vitamin.

SEA BUCKTHORN OIL (Oleum Hippophaeae)

Obtained from the fruits of the Sea Buckthorn, a bush of the family Elaeagnaceae, which grows in various regions of the USSR.

The oil consists of a mixture of the glycerides of oleic, linoleic and palmitic acids, contains vitamin E (110–165 mg%), carotene (40–100 mg%) and carotenoids (180–250 mg%).

Transparent red orange liquid with characteristic odour and taste.

Used externally in treating radiation injuries of the skin, after cleaning the coating from the ulcerous surface the oil is applied with a pipette and the wound dressed with gauze. The dressing is changed each second day. Before applying the oil the ulcerous surface is washed with a solution of penicillin. In radiation therapy of cancer of the oesophagus, patients are prescribed $\frac{1}{2}$ tablespoonful of Sea Buckthorn oil 2–3 times a day during the entire course of treatment and

for 2—3 weeks afterwards. In treating colpitis and endocervicitis Sea Buckthorn oil is applied to the walls of the vagina and the cervical canal by means of cotton balls after preliminary cleansing of the surface. In treating cervical erosion cotton plugs soaked in oil (5—10 ml per plug) are used. The plugs are packed tightly against the eroded surface and are changed daily.

Course of treatment in colpitis — 10—15 applications. In endocervicitis and cervical erosion — 8—12 applications. Treatment is repeated in 4—6 weeks if necessary.

Sea Buckthorn oil can also be used on a par with other oils for the treatment of ulcer of the stomach.

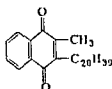
To be stored in bottles filled to the top and well closed in a cool place protected from light.

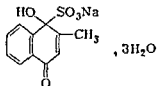
VITAMIN K (Vitaminum K)

Antihemorrhagic or coagulation vitamin. Assists in the formation of prothrombin by the liver and furthers normal coagulation of the blood. The absence or deficiency of vitamin K leads to the development of hemorrhagic manifestations.

Vitamin K is widely distributed in the plant kingdom. Particularly rich sources are green lucerne leaves, spinach, cauliflower, coniferous needles and green tomatoes. Fruit and rootcrops contain much smaller amounts. A certain amount of vitamin K is found in hog liver, milk and eggs contain very little.

Plants contain vitamin K_1 (2 methyl 3 phytyl 1 4 naphthoquinone).





Colourless fine crystalline powder, bitter taste soluble in water

Like other vitamin K preparations, vikazol is a specific therapeutic agent in hemorrhagic disease associated with a low prothrombin content in the blood (hypoprothrombinemia). Its ability of increasing the coagulability of the blood is observed in some cases when there is a normal prothrombin content. The effect of vikazol is manifested within 12—18 hours after administration.

Use: icterus following arrest of flow of bile to intestine; acute hepatitis; parenchymatous and capillary hemorrhage after trauma or surgical intervention; hemorrhage due to ulcer of the stomach and duodenum; pronounced symptoms of radiation sickness; thrombopenic purpura; hemorrhoidal hemorrhage and obstinate epistaxis; prevention of hemorrhagic disease of the newborn by administration to mothers during last month of pregnancy; hemorrhagic symptoms in premature infants; juvenile and preclimacteric uterine hemorrhage; spontaneous hemorrhage; preparation for surgical operations and also in postoperative period if there is danger of hemorrhage; pulmonary hemorrhage resulting from tuberculosis; septic diseases accompanied by hemorrhagic manifestations.

Vitamin K is likewise used as a specific antagonist in excessive hypoprothrombinemia and hemorrhage which may follow the use of dicoumarol and other anticoagulants (vitamin K antagonists).

Vikazol is ineffective in hemophilia and Werlhof's disease.

Administered orally or intramuscularly. Prescribed orally in the form of powders, tablets or aqueous solutions. For intramuscular injections a solution prepared with sterile isotonic saline is used. The daily dose for adults when administered orally is 0.015—0.03 g and when administered intramuscularly — 0.01—0.015 g. The dose for children is lowered according to their age (0.002—0.015 g). The drug is given for 3—4 days in succession followed by a break of 4 days. After the break the administration of vikazol can be renewed for 3—4 days. The daily dose can be given in 2—3 administrations. It is advisable to begin the administration of vikazol 2—3 days prior to operations which are accompanied by severe parenchymatous hemorrhage.

In obstetrical practice, a one day dose of vikazol is given to parturient women immediately after the examination by the physician on their arrival at the maternity hospital if labour has not commenced 12 hours after admission; the dose is repeated at the end of 24 hours it is repeated once more. For the newborn the dose of vikazol should not exceed 0.004 g (oral administration).

Maximal doses for adults: single orally and intramuscularly — 0.015 g, daily orally — 0.03 g, intramuscularly — 0.02 g.

Contraindicated in patients with heightened coagulability of the blood.

Available in powder form: tablets of 0.01, 0.015 and 0.02 g, ampoules containing 1 and 2 ml of 1% solution and 5 ml 0.3% solution.

To be kept in well closed glass containers or sealed ampoules, observing safety precautions (List B).

LINOL (Linolum)

Linol is a mixture of the methyl esters of linoleic, linolenic and oleic acids. Transparent pale yellow liquid, soluble in fatty and mineral oils, ether and benzene; insoluble in water. Specific gravity 0.889—0.900.

According to modern conceptions linoleic and linolenic acids are constituents of vitamin F, which catalyzes the assimilation of fats and prevents or abates dermatitis.

Linol is used for the treatment of skin injuries resulting from radiation therapy. The preparation is applied to the affected surface in a thin layer once a day. Treatment can be by the open method or a gauze dressing moistened with an emulsion of fish liver oil can be applied after the skin has been painted.

To be stored in tightly closed bottles at a maximum temperature of 10° in a place protected from light.

II. AGENTS STIMULATING LEUKOPOIESIS

SODIUM NUCLEINATE (Natrium nucleicum)

Sodium salt of nucleic acid, obtained by the hydrolysis of yeast with subsequent purification. Nucleic acid has a complicated chemical structure. The molecule of the nucleic acid from yeast (ribonucleic acid) contains purine bases (adenine, guanine), pyrimidine bases, a carbohydrate (d ribose) and phosphoric acid.

The sodium nucleinate manufactured for medical use is a white or slightly yellowish powder, soluble in water with the formation of opalescent solutions and insoluble in alcohol, chloroform and other organic solvents. The preparation has the power of stimulating the activity of the bone marrow and causing a leukocytic reaction.

Used in leukopenia and agranulocytosis, as well as in impairment of phosphorus metabolism (phosphaturia, rickets, etc.)

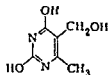
Administered orally and intramuscularly. Orally, adults are given doses of 0.1–0.2 g 3–4 times a day. Doses for children up to 1 year old — 0.005–0.01 g from 2 to 5 years — 0.015–0.03 g, from 6 to 12 years — 0.05–0.1 g.

Intramuscularly, adults are given injections of 5–10 ml 2% or 5% solution once or twice a day. Children — 0.5–5 ml 1% solution. An intramuscular injection of 2–3 ml of 0.5% procaine hydrochloride solution can be given beforehand to lessen the pain.

Duration of treatment 10 days or longer, depending on the course of the disease.

PENTOXYL (Pentoxylum)

5 Methanol-4 methyl uracil



White fine crystalline powder odourless, very slightly soluble in water, more soluble in solutions of alkalis, insoluble in alcohol.

Used to stimulate leukopoiesis in agranulocytic angina, alimentary toxic aleukia, chronic benzene poisoning, leukopenia resulting from the chemotherapy of malignant neoplasms and from the use of radioactive substances, as well as other leukopenic conditions.

According to experimental findings, pentoxyl also stimulates cellular growth in various tissues, accelerates the healing of wounds, intensifies the phagocytic ability of the leukocytes and the reticulo-endothelial system and has an anti-phlogistic effect (N. V. Lazarev).

As in the case of other preparations stimulating leukopoiesis, it is expedient to use pentoxyl only in light forms of leukopenia. In affections of moderate severity the use of leukopoietic stimulants is indicated only after the resumption of the impaired regeneration of blood cells. In severe affections of the hemopoietic system the use of pentoxyl is contraindicated (N. V. Lazarev).

Pentoxyl is administered orally. The length of treatment depends on the effectiveness of the drug and the tolerance shown for it.

The usual single dose for adults is 0.2–0.3 g (up to 0.4 g). Single doses for children up to 1 year old — 0.015 g, from 1 to 3 years — 0.025 g, 3–8 years — 0.05 g, 8–12 years — 0.075 g, over 12 years — 0.1–0.15 g. To be taken 3–4 times a day after meals.

Because of its irritant properties, pentoxyl may cause dyspeptic symptoms. Contraindicated in lymphogranulomatosis and malignant diseases of the bone marrow.

Available in powder form.

To be stored in well closed glass bottles observing safety precautions (List B).

THESAN (Thesanium)

White crystalline powder sparingly soluble in cold water, freely soluble in alcohol. Solutions are stable and withstand sterilization by the usual methods.

Used as a stimulant of leukopoiesis. Indications and contraindications are the same as for pentoxyl.

Administered orally or intramuscularly 3–4 times a day. Taken orally in the form of powders or tablets in doses of 0.01–0.02 g or in the form of a 0.5% solution in 20° alcohol in doses of 10–15 drops. Intramuscularly, injections of 1–2 ml of 0.1–0.5% solution are given.

Information in the literature indicates that in radiation leukopenia thesan is chiefly effective as a prophylactic agent. When administered early and regularly it prevents the development of leukopenia after the onset of leukopenia. The use of thesan arrests its development and fosters the restoration of the leukocyte content.

As a therapeutic agent thesan is effective only in moderate leukopenia.

Course of treatment 10 days or more.

Available in powder form in tablets of 0.01 g and in ampoules containing 1 ml of 0.1 and 0.5% solution.

To be stored in closed glass containers observing safety precautions (List B).

Thesan emulsion. Composition: thesan 0.2%, emulsifier (from the alcohols of spermaceti) 10%, castor oil 10%, water 79.8%. White mass of cream like consistency with characteristic odour.

Used for the prevention and treatment of skin injuries during radiation therapy, ulcers, bedsores and burns.

As a prophylactic the emulsion is applied to the irradiated area of the skin after each treatment.

For the treatment of existing skin injuries the ointment is applied to the affected area in a thin layer by means of a spatula after each irradiation and covered with a gauze napkin through which additional emulsion is applied 2–3 times a day. After completion of the course of radiation therapy application of the emulsion is continued for another 7–10 days.

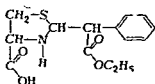
In the treatment of ulcers, burns and the like a gauze napkin well moistened with the emulsion is applied to the affected surface. Dressings are changed each second day or less frequently depending on the indications.

Available in jars.

To be stored in a cool dry place.

LEUCOGEN (Leucogenum)

2 (α-Phenyl α-carbethoxymethyl) thiazolidine-4-carboxylic acid



White crystalline substance sparingly soluble in cold water and alcohol soluble on the addition of sodium bicarbonate. Melting point 158—169°. Aqueous solutions are unstable being hydrolyzed to form l cysteine and formylphenylacetic ether.

Used to stimulate leukopoiesis. Indications and contraindications are the same as for pentoxyl and thesin.

Administered orally in a dosage of 0.02 g 3—4 times a day for adults. The length of treatment depends on the character and course of the disease.

Daily doses for children up to 6 months old — 0.01 g, from 6 months to 1 year — 0.02 g, from 1 to 7 years — 0.01 g, over 7 years — 0.06 g.

Available in powder form and in tablets of 0.02 g.

To be kept in well stoppered bottles in a place protected from light observe safety precautions (List B).

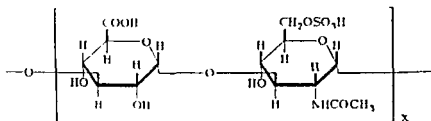
III AGENTS INFLUENCING THE COAGULATION OF THE BLOOD

A Agents inhibiting coagulation

HEPARIN (Heparinum)

Synonyms Iquaeamin Pularin Thromboliquin

Heparin is mucic acid polysulfuric acid — a polysaccharide built up from molecules of hexosamine and hexuronic acid linked with sulfuric acid as esters.



x 10—50

Heparin is a high molecular compound its molecular weight is 15 000—21 000. It is formed in the human and animal organism by the basophil cells.

Contained in the largest amounts in the liver and lungs, smaller amounts occur in the skeletal muscles, spleen and myocardium. Extracted from ox liver and lungs. Put out for medical use in the form of the sodium salt — a white powder, soluble in water.

The activity of heparin is determined by the biological method — by its ability to delay coagulation of the blood — and is expressed in units of anticoagulant activity. 1 mg of international standard heparin possesses 130 units of activity (1 unit = 0.0077 mg). Heparin solutions for injections are available with a potency of 5 000, 10 000 and 20 000 units of anticoagulant activity per ml.

Heparin is a natural anticoagulant factor of the animal organism. It delays the clotting of blood in vivo and in vitro. When introduced into the blood it has an immediate effect.

The anticoagulant action of heparin is due to its ability to inhibit the formation of thrombokinase and lower the readiness of the platelets to agglutinate as well as its ability to bind the thrombin of the blood, converting it into an inactive form. Heparin is considered a direct acting anticoagulant, i.e., one that directly influences the clotting factors in the blood.

The part played by heparin in the organism is not limited to its anticoagulant effect; it also influences other enzymatic processes — in particular, it inhibits

bits the activity of hyaluronidase (see p 283) It has likewise been reported that heparin activates the fibrinolytic properties of the blood enzymes, this may further the resolution of thrombotic masses and accelerate the restoration of patency in plugged blood vessels The administration of heparin also leads to a lowering of the cholesterol content in the blood

In large doses heparin causes dilation of the vessels and lowering of the arterial pressure

Heparin is effective when administered intravenously, intramuscularly and subcutaneously, but the most constant effect is observed when it is administered intravenously When administered orally it is decomposed in the stomach and has no effect

Heparin is quickly decomposed by the body tissues After a single intravenous administration of a therapeutic dose the effect is maintained for 4—6 hours When injected into the vein the inhibition of blood coagulation is immediate when injected intramuscularly or subcutaneously the effect is manifested in 45—60 min, after the effect ceases, the coagulability of the blood is fully restored

Use prevention and treatment of thromboembolic complications in myocardial infarction, operations on the heart and blood vessels thromboembolism of the pulmonary and cerebral vessels, and the central vein of the retina, thrombophlebitis of the extremities, etc

Heparin is also used in blood transfusion and to prevent the clotting of blood in laboratory investigations

The dosage and method of using heparin should be individualized It is usually administered intravenously, the dose for the first few days being 10,000—50,000 units of anticoagulant activity (8—10 ml with an activity of 5,000 units per ml) The daily dose is given in equal parts at intervals of 4—6 hrs, the daily dose is subsequently reduced to 25,000 units

Intravenous administration can be in the form of drip infusions, in this case 5,000 or 10,000 units of heparin are diluted with 500 ml isotonic saline or 5% glucose solution, and infused at a rate of 20 drops per min Sometimes an intravenous injection is given, followed by drip infusion

Intramuscularly and subcutaneously, heparin is administered in the same doses It must be borne in mind that heparin has a local irritant effect and may cause tenderness at the site of injection, as well as hematoma Subcutaneous injections are performed with a fine needle, deep in the subcutaneous tissue

The effect of heparin is checked by blood coagulability determinations

A more detailed study shows that after the administration of heparin a considerable retarding of the recalcification of the plasma occurs, along with a lowering of the tolerance to heparin, lengthening of the thrombin time and a sharp increase in free heparin (owing to that administered) No regular deviations are observed in the prothrombin index or the content of proconvertin and fibrinogen under the influence of heparin

The parenteral administration of heparin is often combined with the oral administration of anticoagulants of the dicoumarol group or phenylin, which differ in their mode of action and in the rapidity of the anticoagulant effect Heparin, which has an immediate effect on the coagulation system of the blood, is usually administered first, subsequently combining it with dicoumarol, neodicoumarin or phenylin, in 3—5 days anticoagulants of the second group are used alone

Contraindications to the use of heparin hemorrhagic diathesis and other diseases accompanied by delayed coagulation of the blood, acute and chronic leukoses and aplastic and hypoplastic anemia, heightened permeability of the vessels, ulcers, polyps and malignant neoplasms of the gastrointestinal tract, subacute bacterial endocarditis, severe impairment of the function of liver and kidneys, operations on the brain and spinal column (danger of postoperative hemorrhage) Heparin must not be administered immediately before an operation When using heparin after operations, deliveries and the like, the possibi-

ility of hemorrhage must be borne in mind, administration of heparin is usually begun 2—10 days after an operation

In blood transfusion, heparin is administered to the donor in a dose of 7,500—10,000 units

To prevent the clotting of blood *in vitro*, 2—3 units of heparin are added per *ml* of blood

In order to prevent the clotting of blood in animals during acute experiments in which the blood pressure is registered, heparin is administered intravenously at a rate of 50—100 units per *kg* body weight

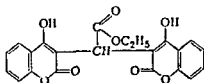
The antagonist of heparin is protamine sulphate, it reverses the effect of heparin and stops hemorrhage 1 *mg* protamine sulphate counteracts 100 units of heparin. Usually 5 *ml* 1% protamine sulphate solution is injected intravenously, if necessary another 5 *ml* is administered in 15 *min*

Heparin is available in hermetically sealed vials containing 5 *ml* solution

To be stored in a place protected from light

NEODICOUMARIN (Neodicoumarinum)

3,3' Carboethoxymethylene bis (4 hydroxycoumarin)



Synonyms Aethylis biscoumacetas, Dicumacyl, Ethylbiscoumacetate, Pelen tan Trombarin, Tromexan

White fine crystalline powder with slight yellowish or greyish tint, odourless almost insoluble in water, slightly soluble in alcohol, sparingly soluble in ether. Melting point 175—178°

Like dicoumarol, neodicoumarin is an anticoagulant which acts indirectly, it is similar to dicoumarol in its mode of action, inhibiting the formation of prothrombin and proconvertin in the liver. Neodicoumarin acts more quickly than dicoumarol, it has less cumulative effect and is less toxic but larger doses are necessary. Indications for use are the same as for dicoumarol. It is administered orally.

As in the case of dicoumarol, treatment should be carried out under careful observation by a physician with an obligatory check at the same intervals on the content of prothrombin and other coagulant factors in the blood. Analyses of the urine are also made regularly for the early discovery of hematuria. The prothrombin index is kept at a level of 40—50%.

During the first few days of treatment 0.3 *g* of the drug is given twice a day, or 0.2 *g* 3 times a day (0.6 *g* in 24 hours), subsequently, 0.15 *g* is given 3 times a day, and then 0.1—0.2 *g* a day.

Maximal doses for adults single — 0.3 *g*, daily — 0.6 *g*

Neodicoumarin can be prescribed in combination with dicoumarol, since the effect of the former is more rapid and that of the latter, more protracted.

According to the method proposed by B. P. Kuschel'sky for the treatment of myocardial infarction, neodicoumarin is administered the first 2 days in a dosage of 0.3 *g* twice a day (trial dose), on the 3rd and 4th days, 0.1 *g* dicoumarol is given once a day (in the morning), and neodicoumarin is given once a day (in the evening) in the following doses, depending on the resistance height: resistance — 0.3 *g*, normal resistance — 0.15—0.3 *g*. If resistance is low, neodicoumarin is not prescribed in the evening. On succeeding days dicoumarol is given in a dose of 0.05—0.1 *g*, depending on the resistance. Resistance is determined by the degree to which the prothrombin content is lowered after the

administration of the trial dose if resistance is normal the prothrombin content is lowered to 40—69% if resistance is low, it is lowered to 20—29%

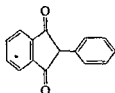
Possible complications assistance to be given and contraindications to use are the same as for dicoumarol

Available in powder form and in tablets of 0.1 and 0.2 g

To be kept locked (List A) in glass bottles tightly stoppered and sealed with paraffin in a dry place protected from light

PHENYLIN (Phenylinum)

2 Phenyl 1,3 indanedione



Synonyms Athrombon Danilone Dindevane Diophindane Emandione Hedulin Phenindione Pindione Thromasal Thrombolyt Thrombophen Trombantin Trombosol

White crystalline powder sparingly soluble in water soluble in alcohol chloroform and ether Melting point 146—147°

Belongs to the group of indirect anticoagulants Similar to dicoumarol and neodicoumarin in its mode of action causes hypoprothrombinemia by inhibiting the process of prothrombin formation in the liver Delay in coagulation of the blood takes place only when phenylin is introduced into the living organism in vitro it has no anticoagulant effect

The effect of phenylin is usually manifested in 18—24 hrs after administration The cumulative effect is less marked than in dicoumarol but more pronounced than in neodicoumarin

Indications for use are the same as for dicoumarol and neodicoumarin

Administered orally For the treatment of thromboembolic conditions 0.03—0.04 g is prescribed 3—4 times a day This dose is indicated for the 1st and 2nd day if the initial prothrombin content is high Then the dose is set individually so as to hold the lowered prothrombin index at a level of 40—50% Usually 0.03—0.04 g is given 2—3 times the next day and subsequently once a day

For the prevention of thromboembolic complications phenylin is usually prescribed in a dose of 0.03 g once or twice a day

Treatment with phenylin is carried out under careful observation by a physician the regular determination of the content of prothrombin and other coagulant factors in the blood being obligatory

In acute thrombosis phenylin is prescribed along with heparin

Possible complications assistance to be given and contraindications are the same as for dicoumarol and neodicoumarin

Because of phenylin's moderate cumulative properties it is easier to regulate the prothrombin level when this drug is used It is tolerated well in therapeutic doses In some patients the palms of the hands assume an orange colour and the urine becomes pink this is due to a chemical transformation of phenylin (transition to the enol form) and is not accompanied by pathological manifestations

Available in powder form and in tablets of 0.02 and 0.03 g

To be kept locked (List A) in a dry place

SODIUM CITRATE for injections (Natrium citricum pro injectione)



Colourless crystals or white crystalline powder, odourless, saline taste, freely soluble in water (1:15), insoluble in alcohol pH of 10% aqueous solution 7.0—7.5

Used in indirect blood transfusion added in the form of a 4—5% solution to prevent clotting

The anticoagulant effect is due to the conversion of the calcium in the blood to calcium citrate, thus binds the free calcium ions which are concerned with the formation of thromboplastin and the transition of prothrombin to thrombin

1

B. Agents accelerating coagulation of the blood

LAGOCHILUS (*Lagochilus inebrians* Bge)

Subshrub of the Mint family (Labiatae), grows in Central Asia

Above ground parts contain lagochillin (tetra atomic alcohol), volatile oil tannin and carotene.

Infusions and tinctures of the flowers and leaves accelerate coagulation of the blood and also act as a sedative

Used to diminish and stop the flow of blood in hemorrhagic diathesis and in uterine, hemorrhoidal, nasal and other hemorrhages, as well as to prevent a heightened tendency to hemorrhage in surgical operations in which large losses of blood may occur

Infusions (1:10 or 1:20) are prescribed orally for adults in a dose of 1 tablespoonful 3—6 times a day, if necessary the dose can be increased to 2 tablespoonfuls 6 times a day 10% tincture (prepared with 96% alcohol) is administered orally to adults in a dose of 1 teaspoonful in 1/4 glass of water 3—5 times a day The infusion (1:10) can also be applied locally, gauze napkins are moistened with the infusion and applied to the bleeding tissues for 2—5 minutes

Lagochilus infusion and tincture have been proposed for use in glaucoma to supplement treatment with miotics (chiefly because of the sedative effect) 1 teaspoonful of 5% tincture or 2 tablespoonfuls of infusion (1:20) are given 3 times a day

Lagochilus preparations are usually tolerated well In individual cases there may be a laxative effect from taking the infusion If the pulse is accelerated the dose should be reduced

NETTLE LEAF (*Folia Urticae*)

Leaves of the wild Nettle (*Urtica dioica* L.), a perennial herb of the family Urticaceae leaves are gathered during the blooming period and dried Contain vitamin C (0.1—0.2%) carotene, vitamin K, tannin, mineral salts and other substances

Used in the form of an infusion or fluid extract as a hemostatic in pulmonary, renal uterine and intestinal hemorrhage Fluid extract of Nettle is often prescribed in combination with fluid extract of Yarrow

YARROW HERB (*Herba Millefolii*)

Dried flowering tops of the common Yarrow (*Achillea millefolium* L.) a perennial herb of the family Compositae, found in dry fields and pastures throughout the Soviet Union

Contains the alkaloid achilleine ($C_{14}H_{26}O_5N_2$), carotene, vitamin C, tannin volatile oil organic acids and resins Judging by experimental findings achilleine increases the coagulability of the blood

Fluid extract and infusion of Yarrow herb are used as hemostatics chiefly in uterine hemorrhage due to inflammatory processes, fibromyoma, etc. Often prescribed together with extract of Nettle leaf

WATER PEPPER HERB (*Herba Polygoni hydropiperis*)

Dried above ground leafy, flowering and fruit bearing stems of Water Pepper (Smartweed — *Polygonum hydropiper* L.), a herb of the Buckwheat family (Polygonaceae) found throughout the USSR Contains rutin quercetin

and other flavonones, and tannin. Reduces the permeability of the vessels and heightens the coagulability of the blood (see Vitamin P).

Used in the form of extract and infusion as a hemostatic, chiefly in uterine hemorrhage. An ingredient of Ethyl Aminobenzoate antihemorrhoidal suppositories.

Fluid extract of Water Pepper (*Extractum Polygoni hydropiperis fluidum*)

Transparent green brown liquid of aromatic odour, taste at first astringent and then bitter. Given in doses of 30—40 drops several times a day.

HYDROPIPERIN (*Hydropiperinum*)

A preparation obtained from Water Pepper Herb freed from ballast matter. Yellow powder without odour or taste, soluble in water, alcohol and chloroform.

Heightens the coagulability of the blood, shortens the duration of hemorrhages and intensifies uterine contractions. Use functional uterine hemorrhage (as an adjuvant in treatment with hormone preparations), uterine fibromyoma, hemorrhage associated with inflammatory processes and insufficient contractive ability of the uterus.

Administered orally in doses of 0.05 g 3 times a day.

Available in tablets of 0.5 g.

To be kept in well stoppered bottles under usual conditions.

CRANBERRYBUSH BARK (*Cortex Viburni*)

Dried bark of trunks and branches of the European Cranberrybush (*Viburnum opulus* L.), a shrub of the Honeysuckle family (*Caprifoliaceae*), gathered in early spring.

Contains the glycoside viburnin, tannin, salts of valeric, formic and caprylic acids, and other substances.

Used as a hemostatic, chiefly in uterine hemorrhage.

Usually administered in the form of a fluid extract, less frequently in the form of a decoction.

Fluid extract of Cranberrybush (*Extractum Viburni opuli fluidum*)

Transparent red brown liquid with characteristic odour and bitter taste. Prepared by percolation of powdered Cranberrybush bark (100 parts to 1 liter 70° alcohol).

Administered orally in doses of 20—40 drops.

ARNICA FLOWERS (*Flos Arnicae*)

Flowerheads of wild and cultivated species of Arnica (*Arnica montana* L., *Arnica foliosa* Nutt. and *Arnica Chamissonis* Less.) perennial herbs of the family Compositae. Flowerheads are gathered at the beginning of the blooming period and dried.

Contain volatile oil, tannin, the bitter principle arnicin, gum, mineral salts and other substances.

Administered in the form of a 10% tincture prepared with 70° alcohol.

Arnica Tincture (*Tinctura Arnicae*)

Transparent greenish brown liquid with characteristic odour and sharp, bitter taste.

Used as a hemostatic in obstetrics and gynecology in cases of insufficient retraction of the uterus and in inflammatory diseases, administered 2—3 times a day. Also has a choleric effect.

IV. HORMONE PREPARATIONS

A. Pituitary preparations

ADRENOCORTICOTROPHIC HORMONE of the pituitary gland (*Hormonum adrenocorticotropinum*, *Corticotropinum*)

Synonyms: Acethrophon, ACTH, Acthar, Acton, Actrope, Adrenocorticotrophin, Cibathen, Cortrophin, Exactin, Solanthyl.

Hormone formed in the basophil cells of the anterior lobe of the hypophysis cerebri. Extracted for medical use from the pituitary glands of swine and oxidized to the maximum of other pituitary hormones. Available in hermetically sealed glass vials in the form of a lyophilic powder, white or slightly yellowish glossy platelets or scales fused in tablets. Freely soluble in water, pH of solutions—3.0—3.5. Stable when dry, undergoes no change over lengthy periods. Solutions are prepared aseptically *ex tempore* with twice distilled water or isotonic saline. When stored under sterile conditions at a maximum temperature of 5° solutions can be used over a period of 2—3 days.

The activity of ACTH is determined by biological methods based on the hormone's power of suppressing lymphoid tissue, in particular the thymus gland or lowering the ascorbic acid content in the adrenals (determinations are made with hypophysectomized rats). The unit of activity is an amount of preparation which when injected subcutaneously in 5—6 day rats causes a 50% reduction in the weight of the thymus gland in 5 days as compared with the weight of the gland in the controls.

ACTH plays an important role in the vital activities of the organism. It is the physiological stimulant of the adrenal cortex and causes the discharge of cortical hormones into the blood stream. This refers particularly to glucocorticoids (hydrocortisone, cortisone, etc.) hormones which regulate carbohydrate and protein metabolism. These hormones suppress the development of lymphoid tissue, inhibit the activity of hyaluronidase, reduce the permeability of the capillaries and have an antiphlogistic effect. They also actively influence other processes proceeding in the body.

The action of ACTH is similar to that of the corticoid hormones, in particular cortisone, but in some cases cortisone and its analogues (prednisone, prednisolone) are more effective. When comparing the effectiveness of ACTH and cortisone administered as medicinal preparations, it must be remembered that ACTH can only mobilize the cortisone and hydrocortisone that the adrenal cortex is able to produce.

ACTH is used in the treatment of rheumatism, infectious, unspecific polyarthritides, gout, bronchial asthma, acute lymphatic and myeloid leukemia, mononucleosis, neurodermatitis, psoriasis, eczema, various allergic disorders and other diseases. Lately ACTH has likewise found application as an agent potentiating antibacterial drugs and improving results in the treatment of tuberculosis (N. A. Shmelyov et al.).

ACTH is usually administered intramuscularly. It is not effective when given by mouth since it is destroyed by the enzymes of the gastrointestinal tract. When injected intramuscularly the preparation is quickly absorbed. The effect of a single intramuscular dose ordinarily lasts 6—8 hrs. Injections are therefore given 3—4 times in 24 hrs. The preparation ACTH zinc phosphate has a more prolonged effect.

In rare cases when a rapid and stronger effect is necessary, the intravenous drip infusion of ACTH solution is permissible. Intravenous administration is performed only at medical institutions.

Doses of ACTH depend for the most part on the character and severity of the disease. In acute rheumatism and in rheumatoid and other forms of arthritis, adults are usually given intramuscular injections of 10—20 units 3—4 times a day. Toward the end of treatment the daily dose is reduced to 20—30 units. In acute rheumatism the course of treatment is 3—4 weeks or more. Usually a total of 800, 1000 or 1200 units is given during the course. When necessary the course of treatment is repeated 2—3 times, with breaks of 1—3 weeks or more. In chronic infectious polyarthritides the course of treatment may last up to 8 weeks or more.

Isotonic saline should not be used in preparing solutions to be administered to patients for whom a saltless diet is indicated.

Children with rheumatism are also given intramuscular injections of ACTH 4 times a day, during the first 2—3 days the daily dose is 20—40 units, then the dose is raised to 40—60 units and toward the end of treatment it is gradually reduced

The therapeutic effect in rheumatism and rheumatoid and other forms of arthritis is manifested in abatement of inflammatory symptoms greater mobility in the joints, lowering of the temperature normalization of the sedimentation rate and improvement in the general condition. A better effect occurs in early forms of the disease, it is less marked in chronic arthritis

When administration of ACTH is discontinued the symptoms of the disease may reappear, renewed administration of ACTH usually gives quick remission. The lengthy uninterrupted use of ACTH is not advisable since it may lead to exhaustion of the adrenal cortex

The administration of ACTH can be alternated with the administration of cortisone and its analogues

In gout, ACTH is usually administered in doses of 10—15 units 4 times a day during the first few days (until acute symptoms have abated) 20—40 units a day is then given for 15—20 days. In bronchial asthma ACTH is prescribed in doses of 5—10 units 4 times a day for 2—3 weeks or more, the total amount coming to 300—1500 units. If there is no effect the dose is increased or recourse is had to intravenous administration. 5—10 units of ACTH dissolved in 500—1000 ml of 5% glucose solution is given by intravenous drip method once a day

In psoriatic erythroderma and arthropathic psoriasis ACTH is administered in a daily dose of 40—100 units, the amount for the course totalling up to 1200 units (M. I. Per et al.)

In leucosis in children ACTH is administered intramuscularly in a daily dose of from 4—5 to 15—30 units (in 3—4 injections). Toward the end of treatment the dose is gradually reduced. Course of treatment from 2—3 to 4—6 weeks. It is considered advisable to alternate injections of ACTH with injections of cortisone (A. F. Tur)

When using ACTH (especially during lengthy administration of big doses) various side effects may be observed: a tendency to retain water as well as sodium and chloride ions in the body, thus giving rise to the development of edema and the elevation of the arterial pressure, tachycardia, excessive intensification of protein metabolism accompanied by a negative nitrogen balance, excitement, insomnia and other disorders involving the central nervous system, moderate hirsutism, upset menstrual cycle. There may be a delay in the cicatrization of wounds and an exacerbation of focal infections in children, growth may be arrested. In diabetes mellitus, intensification of hyperglycemia and the development of ketosis may occur

When the preparation is prescribed correctly side effects are manifested in only slight degree

Treatment with ACTH should be carried out under careful observation by a physician

In order to prevent side effects, it is recommended that the amount of sodium chloride entering the body should be reduced, a diet should be prescribed which is rich in vegetables and fruit (to increase the ingestion of potassium ions) and also rich in protein. In diabetes mellitus the dose of insulin should be increased and lipocain should be administered

Contraindications: severe forms of hypertensive disease and Itsenko—Kushing's disease, pregnancy, decompensated cardiac activity, acute endocarditis, psychosis, nephritis, osteoporosis, ulcer of the stomach and duodenum, recent operations, syphilis, active forms of tuberculosis (in the absence of specific treatment), severe forms of diabetes mellitus, senility

Available in vials hermetically sealed with rubber stoppers, containing 10 or 30 ACTH units

To be stored in a place protected from light, at a temperature of approximately 10°

ACTH ZINC-PHOSPHATE.

An ACTH preparation with a more lasting effect

Administered only intramuscularly One injection takes the place of 3—4 injections of the ordinary ACTH

Put out in the form of two solutions one contained in a vial hermetically closed with a rubber stopper the other in a sealed ampoule. The vial contains 4 ml ACTH solution in 0.01 N HCl with the addition of zinc and a preservative 1 ml represents 25 units of ACTH activity, giving a total of 100 units in the vial The ampoule contains 1 ml of alkaline phosphate solution Before use the liquid in the ampoule is transferred to the vial by means of a syringe the needle being passed through the rubber stopper The contents of the vial are then thoroughly shaken A fine white suspension is formed 1 ml of which contains 20 ACTH units On standing the suspension separates out before being used again it must be thoroughly shaken once more

The effect of the preparation comes on more slowly but is more prolonged than that of ordinary ACTH The maximal effect after a single administration is attained in 9 hrs the effect lasts about 32 hrs

Indications and contraindications are the same as for the ordinary ACTH preparation

To be administered only intramuscularly and not more than once a day in doses of 10 20 or 40 units sometimes 2—3 injections a week are sufficient

The original solutions of ACTH and alkaline phosphate give an active suspension over a period of 4 months from the date of preparation

After mixing the suspension can be kept for 8 days in a cool place

PROLACTIN (Prolactinum)

Names of similar foreign preparations Mammotrophin Physolactin

Preparation of the lactogenic hormone of the anterior lobe of the hypophysis cerebri Extracted from the hypophysis of ox and swine

The hormone is a water soluble protein available in the form of a sterile aqueous solution containing 5 units of activity per ml

Increases the secretion of milk by the mammary glands during the puerperium

Administered intramuscularly Prescribed for primiparae as soon as an insufficiency of milk is evident prescribed for multiparae with history of insufficient lactation the first few days after delivery Administered in a dose of 1 ml twice a day for 5—6 days

To be stored in hermetically sealed vials of 5 ml in a place protected from light at a temperature of 15—20°

INTERMEDIN (Intermedinum)

Melanophore stimulating hormone of the intermediate lobe of the hypophysis cerebri Obtained from pituitary body of cattle

White amorphous powder odourless and tasteless soluble in water (1:20)

Activity is determined biologically by the ability to cause dilation and branching of melanophores in skin of frogs 0.1 mg of the powder contains 1—2 units of activity

Used for the treatment of degenerative changes in the retina (nyctalopia retinitis pigmentosa myopic chorioretinitis) The preparation stimulates the activity of the remaining rods and cones in the retina improves adaptation to darkness and raises acuity of vision

Prescribed in the form of a 5% solution 3 drops to be instilled into the conjunctival sac of each eye (waiting 5 min after each drop before instilling the next)

Treatment is continued for several months solutions are prepared ex tempore

Available in vials containing 0.05 g intermedin ampoules containing 1 ml solvent being provided

To be stored in a cool place protected from light. Solutions can be kept for a maximum of 5—6 days in a cool, dark place

PITUITARY EXTRACT

Names of similar foreign preparations Glandustrin, Hypophen, Hypophysin, Piton, Pituglandol, Pitugan, Pituitrin

Extract of the posterior lobe of the pituitary body (hypophysis cerebri) containing the total hormones Extracted from the pituitary body of cattle

Transparent colourless liquid of acid reaction ($\text{pH}=3.0-4.0$) Preserved with 0.3% solution of phenol or tricresol

The main active principles of pituitary extract are the following hormones 1) oxytocin, which stimulates uterine contractions and is one of the factors ensuring the normal course of labour, 2) vasopressin (pitressin) which contracts the capillaries and raises the blood pressure and 3) antidiuretic hormone, which assists in maintaining the constant osmotic pressure of the blood by increasing the reabsorption of water in the uriniferous tubules and decreasing the reabsorption of chlorides

Oxytocin and vasopressin are octapeptides oxytocin has now been produced synthetically

The biological potency of pituitary extract is determined by its ability to cause contraction of the isolated cornu of the guinea pig uterus 1 ml contains 5 or 10 units of activity

Use stimulation of uterine contractions during labour postpartum hemorrhage, menometrorrhagia, diabetes insipidus nocturnal urinary incontinence

Administered subcutaneously or intramuscularly Dose for adults 1 ml (5—10 units) once or twice a day Dose for children (preparation containing 5 units per ml) up to 1 year old — 0.1—0.15 ml, 2—5 years — 0.2—0.4 ml 6—12 years — 0.4—0.6 ml

In obstetrical practice pituitary extract is administered in divided doses of 0.25 ml every 15—30 min up to a total dose of 1 ml A single dose of 0.5—1 ml can be administered only when there are conditions for the use of obstetrical forceps

Maximal doses for adults single — 10 units daily — 20 units

Maximal doses for children up to 6 months old — 0.5 units (0.1 ml of preparation with potency of 5 units per ml), daily — 1 unit (0.2 ml), from 6 months to 1 year, single — 0.75 units (0.15 ml), daily — 1.5 units (0.3 ml), 2 years, single — 1.25 units (0.25 ml), daily — 2.5 units (0.5 ml), 3—4 years, single — 1.5 units (0.3 ml), daily — 3 units (0.6 ml), 5—6 years single — 2 units (0.4 ml), daily — 5 units (1 ml), 7—9 years single — 3 units (0.6 ml), daily — 7.5 units (1.5 ml), 10—14 years, single — 5 units (1 ml), daily — 10 units (2 ml)

Contraindications marked atherosclerosis, myocarditis, and hypertension and nephropathy of pregnancy In cases of hypertension in parturient women pachycarpine, sphaerophrysine or isoverine can be used instead of pituitary extract to stimulate labour

Available in ampoules of 1 ml containing 5 or 10 units of activity

To be stored in sealed ampoules in a cool place protected from light, observing safety precautions (List B)

Pituitary extract is an ingredient of the preparations antiasthmocrin (see p 116) and mammophysin

ADIURECRIN (Adiurecrinum)

Preparation of posterior lobe of hypophysis Obtained by processing the powdered posterior pituitary of cattle

Fine grey powder, insoluble in water and usual solvents Contains the hormones of the posterior pituitary, in particular the antidiuretic hormone The potency of the preparation is determined biologically 1 mg of adiurecrin represents 1 unit of activity

Used in diabetes insipidus and nocturnal urinary incontinence To be inhaled into the nasal cavity The effect is manifested in 15—20 min In diabe-

les insipidus adiurecrin fosters the disappearance of dryness in the mouth the ending of thirst and the reduction of uresis The action of a single dose of adiurecrin lasts 6—8 hrs, after which inhalation of the preparation should be repeated

Prescribed for adults in doses of 0.03—0.05 g 2—3 times a day, doses for children — 0.005—0.03 g

Infants up to 2 years old are not prescribed adiurecrin

Contraindicated in diseases of the respiratory passages and communicating cavities

To be stored in well stoppered vials in a cool, dry place observing safety precautions (List B)

MAMMOPHYSIN (Mammophysinum)

Mixture of extracts of the posterior pituitary (posterior lobe of hypophysis cerebri) and the mammary gland of cows during lactation

Transparent light yellow liquid of acid reaction Causes rhythmic contractions of the uterus

Used in primary and secondary uterine inertia as well as in hypotonic postpartum hemorrhage and postpartum subinvolution of the uterus

In gynecological practice prescribed in uterine hemorrhage associated with inflammatory processes (metritis adnexitis etc) and in uterine fibromyoma (Y. I. Kvater)

Administered intramuscularly or subcutaneously During labour administered in doses of 0.3—0.4 ml every 30 min until the onset of the effect (a total of up to 6 injections) in other cases 1—1.5 ml is given In uterine hemorrhage injections are given once or twice a day until bleeding ceases In the conservative treatment of fibryoma 1 ml is administered every day for 12—15 days

Contraindications are the same as for pituitary extract

Available in ampoules of 1 ml

B Thyroid gland preparations

THYREOIDIN (Thyreoidinum)

Hormone preparation of thyroid gland Made from dried thyroid glands of cattle

Fine brownish yellow amorphous powder with faint odour characteristic of dried animal tissue Insoluble in water alcohol and other solvents

Possesses biological activity of thyroid gland hormone Standardized according to the content of organic iodine which should be from 0.17 to 0.23%

Used for the treatment of myxedema hypothyrosis cretinism sporadic and endemic goiter obesity and nephrosis

Used in some forms of infantile hypotrophy because of its stimulating influence on tissue respiration Thyreoidin is a specific agent for the treatment of myxedema and hypothyrosis Treatment with thyreoidin timely begun and systematically carried out may lead to the complete disappearance of symptoms of the disease

Administered orally Doses should be carefully individualized taking into account the patient's age and the character and course of the disease

Adults are usually prescribed 0.1—0.2 g 2—3 times a day (in nephrosis up to 1 g daily) Small children are given 0.05—0.1 g daily schoolchildren—0.1—0.2 g daily

Maximal doses for adults single—0.3 g daily—1 g

Maximal doses for children up to 6 months old, single—0.01 g daily—0.03 g from 6 months to 1 year single—0.02 g daily—0.06 g 2 years single—0.03 g daily—0.09 g 3—4 years single—0.05 g daily—0.15 g 5—6 years single—0.075 g daily—0.25 g 7—9 years single—0.1 g daily—0.3 g 10—14 years single—0.15 g daily—0.45 g

Criteria of the correctness of the dose in hypothyrosis are the normalization of the pulse basic metabolism and cholesterol content in the blood

Large doses of thyroïdin may cause symptoms of thyrotoxicosis accelerated pulse, palpitation and sweating. In such cases the dose should be reduced or the preparation withdrawn.

Contraindicated in hyperthyroidism, diabetes and general malnutrition.

Available in powder form and in tablets of 0.1 and 0.2 g.

To be stored in a cool dry place, protected from light, observing safety precautions (List B). Can be stored for 3 years.

C. Parathyroid-gland preparations

PARATHYREOIDIN, Parathyreocrin (Parathyreoidinum, Parathyreocrinum)

Hormone preparation of parathyroids of cattle

Transparent or slightly opalescent brown liquid of acid reaction, pH = 2.5–3.0. Preserved with 0.25–0.3% tricresol solution.

Has the property of increasing the calcium content in the blood and overcoming the tetany syndrome associated with insufficiency of the parathyroid glands. The biological potency is determined by the property of increasing the calcium content in the blood of dogs and is expressed in units of activity. 1 ml contains 20 units.

Used in various forms of tetany, spasmodophilia and allergic diseases (bronchial asthma, urticaria, vasomotor rhinitis, etc.).

Administered subcutaneously or intramuscularly.

In order to abort acute attacks of tetany adults are given injections of 2 ml every 2–3 hrs until convulsions cease, children up to 1 year old are given injections of 0.25–0.5 ml, 2–5 years — 0.5–1.5 ml, 6–12 years — 1.5–2 ml. Simultaneously 5–10 ml 10% calcium chloride solution is administered intravenously or 1 dessertspoonful — 1 tablespoonful of 5% calcium chloride solution is given orally 5–6 times a day.

In other cases parathyroidin is administered in doses of 1–2 ml daily or each second day.

Maximal doses for adults: single — 5 ml, daily — 15 ml.

Maximal single doses for children up to 6 months old — 0.25 ml; from 6 months to 1 year — 0.4 ml, 2 years — 0.6 ml, 3–4 years — 0.8 ml, 5–6 years — 1 ml, 7–9 years — 1.5 ml, 10–14 years — 2 ml.

Contraindicated in hypercalcaemia. During treatment with parathyroidin blood examinations for calcium must be made.

Available in ampoules of 1 ml and in hermetically sealed vials of 5 and 10 ml.

To be kept in a cool place protected from light, observing safety precautions (List B).

D. Pancreas preparations and their synthetic analogues

INSULIN (Insulinum)

Insulin is the hormone contained in the β cells of the islets of Langerhans in the pancreas. It has an antidiabetic effect. It is a high molecular protein (molecular weight = 35 000), built up from 10 amino acids, contains 12% cysteine.

Insulin preparations for medical use are obtained by extracting the pancreas of cattle. Solutions are prepared by dissolving the insulin in water acidified with hydrochloric acid. They are preserved with a 0.3% solution of tricresol or phenol. Potency is determined biologically. The unit of activity is the specific activity of 0.0408 mg crystalline insulin (the ability to cause a reduction in the amount of blood sugar in healthy rabbits).

Insulin solution is a transparent, colourless, sterile liquid with the odour of the preservative. Contains 16–18% glycerine. pH = 2.5–3.5.

Insulin has an active influence on carbohydrate metabolism, it lowers the blood sugar concentration and promotes the assimilation of carbohydrates by the tissues (1 unit of insulin promotes the assimilation of about 4 g of sugar).

Used in diabetes mellitus (while simultaneously following a rational diet).

Doses are individualized depending on the patient's condition and the concentration of sugar in the urine (at the rate of 1 unit of insulin per 5 g sugar excreted in the urine.) Doses usually range from 10 or 20 to as much as 40 units a day. When changing doses analyses of the urine are made to check the sugar concentration. In diabetic coma the dose of insulin may reach 100 units or more daily.

Insulin is administered subcutaneously or intramuscularly. Intravenous injections (up to 50 units) are given only in diabetic coma in cases in which subcutaneous injections do not give the required effect.

Subcutaneous injections of insulin are given 30—60 min before meals. The action of a single injection lasts about 6 hrs, if necessary 2—3 injections are given daily.

Small doses of insulin (5—10 units) are used in cases of emaciation, malnutrition, furunculosis, thyrotoxicosis, excessive vomiting of pregnancy, diseases of the stomach (atony, gastroparesis), hepatitis and early forms of cirrhosis of the liver (with the simultaneous administration of glucose). Insulin is also used in some forms of mental diseases such as schizophrenia (20—80 units).

Caution must be observed when using insulin. Overdosage of insulin and the untimely ingestion of carbohydrates may cause hypoglycemic shock with loss of consciousness, convulsions and depression of cardiac activity. On the appearance of symptoms of hypoglycemia the patient must be given 100 g of white bread or biscuits and if symptoms are more pronounced 2—3 big spoonfuls of granulated sugar. In hypoglycemic shock 50 ml of 40% glucose solution is injected intravenously followed if necessary by intravenous drip infusion of 5% glucose solution or the administration of 500 ml of this solution subcutaneously and in the form of an enema. A subcutaneous injection of 1 ml 0.1% adrenalin hydrochloride is also given.

Insulin is contraindicated in patients with a tendency toward hypoglycemia.

Great caution is necessary in patients with diabetes mellitus if there are symptoms of coronary insufficiency and impairment of cerebral blood circulation.

Insulin is available in sterile vials hermetically closed with rubber stoppers containing 5 and 10 ml of solution having a potency of 20, 40 or 80 units per ml.

In order to draw the insulin into a syringe the needle is passed through the rubber cap after swabbing off the latter with alcohol or tincture of iodine.

To be stored in a cool place (at a temperature not higher than 10°), observing safety precautions (List B).

ZINC INSULIN SUSPENSION

Mixture of highly purified amorphous insulin and crystalline zinc insulin in the proportion of 1 : 4 in an acetate buffer solution. Preserved with 0.2% triethanolol. When shaken forms a fine suspension which settles out on standing; the liquid above the white sediment is transparent and colourless. 1 ml of the suspension contains 40 units of insulin. Has a slower and more prolonged action than ordinary insulin. The effect of a single subcutaneous injection lasts up to 24 hrs.

Indicated in moderate and severe forms of diabetes mellitus requiring more than 40 units of insulin per day when 2—3 injections of ordinary insulin would be necessary. In such cases $\frac{2}{3}$ of the insulin can be replaced by suspension.

The preparation is only administered subcutaneously; intravenous injections are impermissible. Not used in precomatose and comatose conditions in patients disposed to acidosis or in nondiabetic conditions.

Available in vials of 5 and 10 ml hermetically closed with rubber stoppers.

To be stored in a cool place.

PROTAMINE ZINC INSULIN (Protamin zinc insulinum)

Long acting insulin preparation in the form of a suspension. Made by adding a solution of protamine zinc chloride and sodium phosphate to a solution of crystalline insulin.

Sterile white aqueous suspension when shaken there should be no large particles. On standing the suspension settles out with the formation of a white sediment and a colourless liquid. Preserved with a 0.25–0.3% solution of tricresol or phenol. pH of suspension = 6.9–7.3.

The potency is determined biologically. 1 ml contains 40 units of insulin activity.

Protamine zinc insulin has a slower and more lasting effect than ordinary insulin. The lowering of the blood sugar concentration persists for 12–24 hrs after administration. Only subcutaneous injections are used. Intravenous administration is impermissible.

Used only in the treatment of diabetes mellitus (while simultaneously following a rational diet).

Doses are fixed individually and range from 20 to 60 units depending on the severity of the disease.

In moderate and severe forms of diabetes mellitus when injections of ordinary insulin must be given 3–4 times a day $\frac{2}{3}$ of the total amount is replaced by a single injection of protamine zinc sulphate. $\frac{1}{3}$ of the amount is made up with ordinary insulin which is administered until the onset of the action of the protamine zinc insulin. The preparation is not used in precoma and coma conditions or in patients disposed to acidosis.

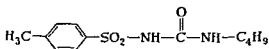
Available in vials of 5 and 10 ml.

Before drawing the preparation into the syringe the vial must be shaken until a uniform suspension is formed.

To be stored in a cool place protected from light.

BUTAMID (Butamidum)

N (4-Methylbenzenesulfanyl) N-n-butylcarbamide



Synonyms: Aglycid, Arcosol, Artosin, Beglucin, D 860, Diabetamid, Diabetol, Dirastan, Dolipol, Mobenol, Neoinsoral, Orabet, Oresan, Orinase, Rastinon, Tolbutamide, Tolglybutamide, Tolumid, Toluvan.

White crystalline powder, insoluble in water, soluble in alcohol, forms freely soluble salts with alkalis. Melting point 128.5°–129.5°.

Butamid is a synthetic sulfonamide drug which has the ability to lower the blood sugar concentration in patients with diabetes mellitus and reduce the amount of sugar excreted in the urine. Unlike sulfanilamide drugs, butamid has no NH₂ group attached to the benzene nucleus and consequently has no antibacterial action; it does not inhibit the microflora of the intestine and is not subject to acetylation.

The mode of action of butamid and analogous drugs is not sufficiently clear. It is assumed that they depress the α cells of the islets of Langerhans in the pancreas, in this way decreasing the production of glucagon, which is the antagonist of insulin. According to other findings, they stimulate the β cells and intensify the secretion of insulin. It has likewise been reported that they inhibit the insulinase of the liver, an enzyme that hydrolyzes insulin (S. M. Leites and N. P. Smirnov). An inhibition of other enzymes concerned in carbohydrate metabolism is also observed. The opinion has also been advanced that what is most important in the action of the antidiabetic sulfonamides is their influence on the liver, the depolymerization of glycogen to glucose being diminished (S. G. Genes).

Butamid is used for the treatment of diabetes mellitus chiefly in patients more than 45 years old with a duration of the disease of not more than 5 years, in whom disturbed carbohydrate metabolism can be regulated with insulin in doses of 40–60 units or in patients who do not use insulin at all. Treatment

with butamid is less successful in persons who use insulin in higher doses and in whom the disease is of long duration as well as in patients younger than 45

Doses should be individualized taking into account the severity of the diabetes and the effectiveness of treatment. Usually the preparation is given in the following doses: 1st day — 1.5–3 g (3–6 tablets of 0.5 g), 2nd day — 1–2.5 g (2–5 tablets), 3rd day — 0.5–2 g (1–4 tablets), 4th day and onwards — 0.5–1.5 g (1–3 tablets). In most patients these doses ensure the rapid build up of the necessary concentration of the drug in the blood; this is maintained by the administration of smaller doses (0.2–1 g daily).

Maximal doses for adults: single — 1.5 g daily — 1 g

Butamid is taken half an hour after meals. If the daily dose does not exceed 1 g it is given in a single administration. If it exceeds 1 g it is given in 2 administrations (after breakfast and dinner).

Treatment with butamid should be carried out under the careful observation of a physician and patients should follow a diet. Regular determinations must be made of the concentration of sugar in the blood (in the morning on an empty stomach) and in the 24 hour urine. Before beginning treatment and during the first few days of treatment these examinations must be carried out every day. During treatment general examinations of the blood must be made regularly.

Insulin can be withdrawn at once (if the dose does not exceed 20 units per day) or gradually part of the insulin being replaced by butamid roughly 10 units of insulin can be replaced by 0.5 g butamid (1 tablet). A conclusion as to whether or not it is possible completely or partially to replace insulin is drawn however on the basis of laboratory examinations (the concentration of sugar in the blood and urine) and the patient's general condition.

Contraindications: mild forms of diabetes compensated by the diet in children and adolescents; precoma and coma; tendency to obesity; diseases of liver and kidneys with impairment of function; acute infectious diseases; leukaemia and thrombopenia; pregnancy; surgical operations; heightened sensitivity to sulfonamide drugs.

Butamid is only slightly toxic but side effects may occur in some cases: headache, dyspeptic symptoms, allergic reactions (pruritus, dermatitis), leukaemia and thrombopenia. If necessary the dose of butamid is reduced; if side effects are persistent a shift is made to treatment with insulin.

If hypoglycaemia should develop (because of overdosage or heightened sensitivity) glucose is administered and the same measures are resorted to as in overdosage of insulin.

If butamid is not sufficiently effective the administration of insulin is renewed.

Available in powder form and in tablets of 0.5 g.

To be stored in a place protected from light observing safety precautions (List B).

Rp Butamid 0.5

D t d N 20 in tabul

S 1 tablet once a day

LIPOCAIN (Lipocainum)

A preparation of the lipotropic substance of the pancreas. Obtained from the pancreas of the ox after extracting the insulin. Contains the so-called "Lipocaine" substance.

Similar preparations are put out abroad under the names Biolipe, Liphormone and Lipotrat.

Slightly yellowish powder, soluble in water.

Potency is determined biologically: 1 g of the dry preparation contains 100 units of activity.

Lipocaine can be considered the second hormone of the pancreas, the first being insulin. It inhibits the development of fatty infiltration of the liver and

stimulates the action of lipotropic substances in respect to their influence on the formation of phospholipids and the escape of the latter from the liver into the blood (see Choline and Methionine) Lipocain activates the metabolism of phospholipids and the oxidation of fatty acids in the liver (S. M. Leites)

Used in diseases of the liver (hepatitis, Botkin's disease, fatty dystrophy, cirrhosis), and in diabetes mellitus with a tendency toward ketosis. It has been reported that lipocain has a beneficial influence in coronary atherosclerosis (abatement of the pain in the region of the heart and favourable changes in lipid metabolism values)

Administered orally in a dosage of 0.1–0.2 g (1–2 tablets) 2–3 times a day in courses of 10–20 days

For the maximal therapeutic effect from lipocain it is necessary simultaneously to prescribe such lipotropic substances as methionine, choline, or food stuffs containing the lipotropic factor for example curds (up to 200 g per day) or oatmeal porridge

Available in powder form and in tablets of 0.1 g

To be stored in a dry place at a maximum temperature of 15–18°

E. Preparations of female sex hormones and their synthetic analogues

a) Estrogenic preparations of steroid structure

FOLLICULIN, ESTRONE (Folliculinum, Oestronum)

Folliculin or estrone is a natural follicular hormone necessary for the normal development of the female organism. It begins to be produced in the ovaries at the onset of the period of sexual maturation being formed in the ripening follicles until the beginning of the climacteric

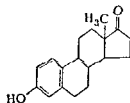
Along with the hormone of the corpus luteum, the follicular hormone is concerned in accomplishing the menstrual cycle. Both hormones are necessary for the function of childbearing in women

Estrone is one of the follicular hormones. Other hormones are also formed in the female body which are similar in action to estrone (estradiol and others). These hormones are called estrogens or estrogenic substances because they cause estrus (or "heat") in castrated female laboratory animals (mice or rats)

Estrone for medical purposes is extracted from pregnancy urine of women or animals. During pregnancy the production of the follicular hormone increases considerably and large amounts are excreted in the urine

In the pure form estrone is a crystalline substance soluble in ether and absolute alcohol, more soluble in acetone and oil, almost insoluble in water. Melting point 254–259°

In chemical structure, estrone belongs to the steroid hormones. It has the following structure



Synonyms: Cristallovat, Estrone, Estrugenone, Estrusol, Femidin, Folest-rin, Glandubolin, Gynoeseryl, Hiestron, Ketodestrin, Ketohydroxyestratriene, Ketohydroxyestrin, Menformon, Oestrin, Oestrobion, Oestroglandol, Oestrogynon, Perlatan, Progynon, Theelin, Thelestrin, Thelykinin, Tokokin, Unden

When introduced into the body, folliculin has a specific action characteristic of estrogenic preparations: it causes proliferation of the endometrium, stimulates the development of the uterus and secondary female sexual characteristics when these are undeveloped, abates and overcomes general disorders that arise in the woman's body due to ovarian insufficiency during the climacteric or following gynecological operations.

The potency of folliculin is determined biologically by the ability to produce estrus in castrated females (mice or rats). 1 mg folliculin contains 10 000 units.

Like other estrogenic preparations, folliculin is used in pathological conditions associated with ovarian insufficiency: underdevelopment or atrophy of the genitals and mammary glands, absence or disturbance of menstruation, climacteric or postcastration disorders, sterility, uterine inertia, past term pregnancy, etc. Also used in the treatment of hypertension during the climacteric, and at times in spasms of the peripheral vessels.

Administered intramuscularly in the form of oil solutions.

In primary amenorrhea with underdevelopment of the genital organs and secondary sexual characteristics, 10 000–20 000 units are administered daily or each second day over a period of 1–2 months or more until the uterus enlarges perceptibly. Progesterone is then administered intramuscularly in a dose of 5 mg daily for 6–8 days. When necessary courses of hormone therapy are repeated. In secondary amenorrhea 10 000 units of estrone are administered daily for 15–20 days, followed by the administration of progesterone or pregnin for 6–8 days in the dose indicated above. If there is no persistent effect the course of treatment is repeated.

In hypo- and oligomenorrhea, algomenorrhea (or dysmenorrhea), and sterility due to hypofunction of the ovaries and underdevelopment of the uterus, administration of folliculin is begun at the end of menstruation, 5 000–10 000 units are given daily for 15–20 days, after which in the presence of indications progesterone or pregnin is administered for 6–8 days in the dose indicated above. In the presence of indications this course of treatment is repeated several times during the same period after the end of menstruation.

In pathological manifestations associated with the onset of the climacteric or with the excision of the ovaries (angioneurotic symptoms, depression, etc.) 1 000, 5 000, or 10 000 units are given daily or each second or third day in courses of 10–15 injections. If symptoms reappear the course of treatment is repeated.

In uterine inertia and past term pregnancy, folliculin is given 2–3 hrs before the administration of labour accelerating drugs. 40 000–50 000 units are administered intramuscularly. Hexestrol can be used instead of folliculin.

Folliculin and all other estrogenic preparations are contraindicated in malignant and benign neoplasms of the genitals, mammary glands and other organs, mastopathy, endometritis, tendency toward uterine bleeding, as well as the hyperfollicular stage of the climacteric.

Too prolonged use of folliculin or other estrogenic preparations may lead to uterine bleeding.

Treatment with folliculin and all other estrogenic hormones should be carried out under the careful observation of a physician.

Available in oil solution in sealed ampoules of 1 ml containing 0.5 and 1 mg folliculin, i.e., 5 000 or 10 000 units in 1 ml.

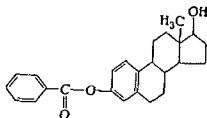
Available in alcoholic solution (1 ml = 1000 units) in vials of 30 ml for external application (to be rubbed into the skin) in acne vulgaris and acne rosacea, and in virile hypertrichosis in women. Dose for external use—20–30 drops.

To be kept in a cool, dry place protected from light.

ESTRADIOL MONOBENZOATE (Oestradiolum monobenzoicum, Oestra-

diol(benzoas)

Ester of estradiol one of the female sexual (estrogenic) hormones and benzoic acid



Synonyms Benzesirin Benzhormovarine Dimenformon benzoate Diogyn B Disynformon Estradiol benzoate Follidrin Gynformone Metroval Oestrin Oestroform Ovocylin benzoate Progynone B Provetan

White crystalline substance soluble in vegetable oils and alcohol almost insoluble in water

Estradiol is formed in the female body along with folliculin. It possesses high estrogenic activity. 1 ml estradiol monobenzoate corresponds to 10 000 units.

In the form of esters (monobenzoate or dipropionate) estradiol is only slowly decomposed in the body tissues and is therefore convenient for parenteral administration. Esters of estradiol are slowly absorbed and slowly excreted and have a relatively prolonged influence on the body; they can for that reason be administered at relatively long intervals.

Indications and contraindications are the same as for folliculin. Estradiol monobenzoate is administered intramuscularly in the form of a 0.1% oil solution.

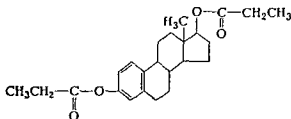
Single dose — 0.001—0.0015 g (1—1.5 mg) injections are given once in 3—5 days.

Available in ampoules containing 1 ml 0.1% oil solution (1 mg estradiol monobenzoate).

To be stored in a place protected from light, observing safety precautions (List B).

ESTRADIOL DIPROPIONATE (Oestradiolum dipropionicum) •

Ester of estradiol and propionic acid



Synonyms Dimenformon dipropionate Diogyn Diocycilin Estradiol dipropionate Ovocylin dipropionate Progynon DP Synformon

Crystalline substance soluble in vegetable oils, alcohol and ether, insoluble in water.

The preparation has a strong estrogenic action which is slow in onset and prolonged.

Indications and contraindications are the same as for folliculin and estradiol monobenzoate.

Administered intramuscularly in the form of a 0.1% solution in oil in a dose of 1 ml 2—3 times a week

The schedule and length of treatment depend on the character of the disease and the effectiveness of treatment etc (see Folliculin)

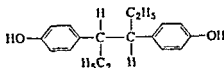
Available in ampoules containing 1 ml 0.1% solution (1 mg estradiol dipropionate)

To be stored in a place protected from light observing safety precautions

b) Estrogenic preparations of nonsteroid structure

HEXESTROL (Hexoestrolum)

3,4-Bis (p hydroxyphenyl) hexane



Synonyms Dihydrostilbestrol Estrene Estronal Folliplex Hexanestrol Hormonoestrol Mesohexostrol Novostro¹ Synestrol Syntex Synthovo

White or slightly yellowish crystalline powder odourless freely soluble in alcohol and chloroform soluble in oils (1:50) insoluble in water Melting point 181—186°

Hexestrol is a synthetic compound — a derivative of stilbene It differs from the steroid estrogenic hormones in chemical structure but is similar to them in biological and therapeutic properties Diethylstilbestrol oestrol and other synthetic estrogenic preparations also belong to the group of stilbene derivatives

In estrogenic activity hexestrol is equal to estrone 1 mg synestrol corresponds to 10 000 units

Indications for the use of hexestrol in women are basically the same as for folliculin

Hexestrol is likewise used in hypertrophy and cancer of the prostate in males (according to the method proposed by A. B. Topchan and A. A. Pomerantsev)

Administered intramuscularly subcutaneously in the form of oil solutions and orally in tablets and alcoholic solutions Hexestrol is quickly absorbed when administered by mouth it is not decomposed in the gastrointestinal tract

Patients suffering from hypogonadism and congenital amenorrhea and with pronounced underdevelopment of the uterus are prescribed 1—2 mg intramuscularly or 2 mg orally per day over a period of 4—6 weeks or more In the presence of an effect (increase in the size of the uterus and mammary glands etc.) progesterone is then prescribed (5 mg daily intramuscularly) or pregnen (10 mg orally 3 times a day) over a period of 6—8 days If necessary these courses of hormone therapy are repeated In secondary amenorrhea hexestrol is administered in a dose of 1—2 mg a day for 15—20 days followed by progesterone or pregnen for 6—8 days in the doses indicated

In hypo- and oligomenorrhea the preparation is administered in a dose of 1 mg intramuscularly or orally daily or each second day during the first half of the intermenstrual period in sterility due to underdevelopment of the uterus 1 mg is given intramuscularly or 1—2 mg orally during the first 7—8 days after menstruation in climacteric disorders with cardiovascular and nervous disturbances 0.5 mg is administered daily for 10—12 days If necessary the course of treatment can be repeated

Hexestrol is also used to increase the effectiveness of agents for stimulating labour (see Folliculin) 1—2 ml 0.1% solution is injected intramuscularly (repeated if necessary)

In hypertrophy of the prostate, 2—3 ml 2% hexestrol solution is administered intramuscularly every day. Administration is continued for 2—3 months followed by a break of 3—4 months. These courses of treatment are repeated over a period of 2—2½ years until dysuric symptoms abate and the prostate decreases in size.

Hexestrol and other estrogens are likewise used in the treatment of patients with some forms of malignant neoplasms (often in conjunction with other methods of treatment: surgical, roentgenotherapy, etc.).

In cancer of the prostate 2—3 ml 2% solution is injected intramuscularly every day for 2—3 months, after a break of 2 weeks injections are resumed in a dose of 0.01—0.02 g daily (0.5—1 ml 2% solution) for 5—6 months. Treatment is lengthy — over a period of several years.

Hexestrol is also used in treating cancer of the mammary gland (F. M. Lampert). The preparation is prescribed for women over 60 years old, in women under 60 androgenic preparations are used (see Testosterone propionate and Methyltestosterone). 2% hexestrol solution is administered intramuscularly every day, beginning with a daily dose of 1 ml and gradually increasing this to 5 ml. The optimal dose is fixed by careful observation and is administered over a lengthy period.

Maximal doses for adults orally, single — 0.002 g daily — 0.004 g, intramuscularly, single — 0.002 g (2 ml 0.1% solution), daily — 0.003 g. In treating malignant neoplasms it is permissible to administer up to 0.1 g intramuscularly per day (5 ml 2% solution).

Contraindications are the same as for folliculin, hexestrol should not be prescribed in cases of impaired function of the liver.

Hexestrol is usually tolerated well, and side effects occur only in rare cases in the form of nausea, vomiting and vertigo.

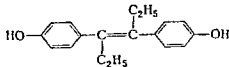
Available in tablets of 0.001 g (1 mg) and in ampoules containing 1 ml 0.1% oil solution (1 mg synestrol) and 1 ml 2% oil solution (20 mg synestrol).

The 2% solution is to be used only in treating patients with malignant neoplasms.

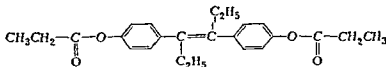
To be stored in a place protected from light, observing safety precautions (List B).

DIETHYLSTILBESTROL and DIETHYLSTILBESTROL DIPROPIONATE
(Diaehtylstilboestrolum, Diethylstilboestrolum, Diaehtylstilboestrolum dipropionicum)

Diethylstilbestrol is 3,4 di p hydroxydiethylstilbene (or trans 3,4 di p hydroxyphenyl) hexene 3); diethylstilbestrol dipropionate is the dipropionic ester of this compound.



Diethylstilbestrol



Diethylstilbestrol dipropionate

Synonyms of diethylstilbestrol: Agostilben, Comestrol, Cyren A, Distilbene, Estilbin, Estrobene, Estrofix, Estromenin, Estromonum, Fonatol, Gynopharm,

Hormostilboral, Neocestrol, New oestrol, Oestramon, Oestrogenin, Oestromin, Oestrosynal, Ovendosyn, Pabestrol, Stilbarol, Stilbestrol, Stilbetin, Stilboestroform, Stilboestron, Stilbofolin, Stilboral, Synestrin, Synthocrin, Synthoestrin, Syntofolin

Synonyms of diethylstilbestrol dipropionate: Clinestrol, Cyren B, Dibestil, Estilben, Estril, Estrobene DP, New oestrol II, Oestilbrol, Oestramenol, Oestrol, Oestrostilbene, Pabestrol D, Sinestrol, Stilbestrol D, Stilbestronate, Synoestren, Syntestrin, Synloestron

Diethylstilbestrol: white crystalline powder, soluble in alcohol, ether, chloroform, fatty oils and dilute solutions of alkalis, very sparingly soluble in water. Melting point 168—172°

Diethylstilbestrol dipropionate: crystalline powder, soluble in ether and chloroform, sparingly soluble in alcohol, almost insoluble in water. Melting point 101—107°

Both drugs are prepared synthetically. They have greater estrogenic activity than folliculin and hexestrol. 1 mg diethylstilbestrol contains 20,000 units of activity. Diethylstilbestrol is somewhat more toxic than hexestrol.

Diethylstilbestrol is administered intramuscularly and by mouth. Solutions of diethylstilbestrol dipropionate are administered intramuscularly; they have a more prolonged action and injections can be given at longer intervals than solutions of diethylstilbestrol.

Indications for the use of diethylstilbestrol and diethylstilbestrol dipropionate are the same as for folliculin and hexestrol, because of their greater potency they can be used in more pronounced pathological conditions. Diethylstilbestrol is also used in some diseases not directly associated with changes in the endocrine system, for example, in ulcer of the stomach and duodenum, in endarteritis obliterans, etc.

In hypogonadism and primary amenorrhea diethylstilbestrol is administered in doses of 0.001 g (1 mg) twice a day, diethylstilbestrol dipropionate is administered in doses of 0.005 g (5 mg = 1 ml 0.5% oil solution) once in 3—4 days. Treatment is continued for 4—6 weeks or more. If there is a therapeutic effect progesterone is then administered intramuscularly, 0.005 g daily for 6—8 days or pregnin is given orally 0.01 g 3 times a day for the same period. If necessary the course of treatment is repeated 4—6 times.

For patients with secondary amenorrhea and with somewhat underdeveloped uterus diethylstilbestrol is prescribed in a daily dose of 0.001 g (1 mg) in the form of injections or tablets, or diethylstilbestrol dipropionate is given in the form of injections of 1 mg each second day. Treatment is continued 2—3 weeks, after which progesterone is given, 5 mg daily for 6—8 days, or pregnin 30 mg daily, for the same period.

In hypo-oligomenorrhea both drugs are only given for 12—15 days during the phase of proliferation of the endometrium, i.e., during the first half of the intermenstrual cycle. Diethylstilbestrol is administered in a daily dose of 0.5—1 mg, and diethylstilbestrol dipropionate is given in the same dose each second day. In climacteric disturbances, diethylstilbestrol is administered orally in a daily dose of 0.25—0.5 mg for 10—15 days; if necessary the course of treatment is repeated after a break of 3—4 weeks.

When there are indications for suppressing lactation after delivery, diethylstilbestrol is given in the form of tablets 5 mg 2—3 times a day for 2—3 days or intramuscularly, 5 mg once or twice a day.

In treating patients with cancer of the prostate, surgical enucleation of the parenchyma of the testes is first performed. During the first course of treatment patients receive daily injections of 40—60 mg diethylstilbestrol intramuscularly (up to 2 ml 3% oil solution) until the appearance of a tender swelling of the mammary glands but at least 30 days. When the tenderness has disappeared and the swelling has abated (these symptoms are the result of the first course of injections), the second course of treatment is begun. The dose for the second course of treatment is fixed on the basis of the condition of the prostate and the

presence of metastases and associated pain. Usually the second course of treatment consists in daily intramuscular injections of 30 mg diethylstilbestrol for 30—40 days. After the second course, treatment is discontinued or diethylstilbestrol is given orally in tablets, 10 mg per day, depending on the patient's condition. In subsequent treatment the character of the changes in the prostate and the condition of metastases serve as a guide.

Diethylstilbestrol is also used in the treatment of cancer of the mammary gland in women. Like hexestrol, it is only prescribed for women more than 60 years old. Because of the high potency of diethylstilbestrol, doses should be reduced to $\frac{1}{3}$ — $\frac{1}{2}$ of hexestrol doses.

When using diethylstilbestrol for the treatment of thrombangitis and endarteritis obliterans, it is injected intramuscularly 0.002—0.003 g (2—3 mg) each second day, the course of treatment consists of 40 injections. Administration of the drug brings about an improvement in the collateral circulation. In ulcer, 0.001 g (1 mg) is administered each second day, the course consisting of 8—12 injections. Diethylstilbestrol is not used in cases of bleeding ulcers.

Maximal doses of diethylstilbestrol for adults orally single—0.001 g, daily—0.003 g; intramuscularly single—1 ml 0.1% solution, daily—3 ml 0.1% solution. In the treatment of malignant neoformations the daily administration of 2 ml 3% solution is permissible.

Contraindications to the use of diethylstilbestrol and its dipropionate in women are the same as for folliculin. These drugs should not be prescribed in diseases of the liver and kidneys.

Treatment must be carried out under the careful observation of a physician. If administration is too long and if large doses are used, there may be (just as when hexestrol is used) excess proliferation and cystoglandular degeneration of the endometrium, and injury to the liver.

In the usual doses side effects are observed only in isolated cases: nausea, vomiting, epigastric pain, headache and heightened libido. In such cases the dose should be reduced or the drug withdrawn or replaced by a steroid estrogen (folliculin, estradiol dipropionate or estradiol monobenzoate).

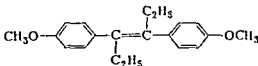
Diethylstilbestrol is available in tablets of 0.001 g (1 mg) and in 1 ml ampoules containing 0.1% and 3% oil solution (1 mg or 30 mg diethylstilbestrol per ampoule). The 3% solution is to be used only in treating patients with malignant neoformations.

Diethylstilbestrol dipropionate is available in 1 ml ampoules containing 0.1% and 0.5% oil solution (1 mg or 5 mg diethylstilbestrol dipropionate per ampoule).

Both drugs are to be stored in sealed ampoules or tightly closed glass bottles in a place protected from light, observing safety precautions (List B).

DIMESTROL (Dimoestrolum)

Diethylstilbestrol dimethyl ether (p dimethoxy 3,4 diethylstilbene)



Synonyms: Depot Cyren, Depot Ostromenon, Depot Ostromon, Dimethyl-Oestrogen, Ostrastilben (D).

White crystalline powder, characteristic odour, soluble in alcohol, ether, chloroform and vegetable oils, insoluble in water.

Prepared synthetically. Has a more prolonged action than hexestrol and diethylstilbestrol. Because of its lasting effect can be administered at longer intervals than other drugs of this series.

Used in ovarian deficiency. Indications are the same as for hexestrol and diethylstilbestrol.

Administered intramuscularly in the form of a 0.6% oil solution. Doses are individualized depending on the peculiarities of the case and the effectiveness of treatment. Usually one injection of 12 mg (2 ml solution 21 000 units) is given per week course of treatment—2–3 injections. The effect of the first injection is usually manifested on the 3rd–6th day.

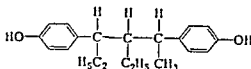
Contraindications and possible complications when using diethylstilbestrol dimethyl ether are the same as when using other synthetic analogues of folliculin.

Available in ampoules containing 2 ml 0.6% oil solution (12 mg dimestrol per ampoule).

To be stored in a place protected from light observing safety precautions (List B).

OCTESTROL (Octoestrolum)

3 Ethyl 2,4 bis (p hydroxyphenyl) hexane



Synonyms Benzeztrolum Octofololin

White crystalline powder, practically insoluble in water, freely soluble in alcohol and vegetable oils. Melting point 160–162°.

Octestrol is a synthetic drug which, like hexestrol, has a pronounced estrogenic action when taken orally. Similar to hexestrol in potency, 1 mg represents 10 000 units of activity.

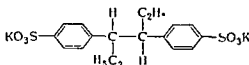
Indications, contraindications and doses are the same as for hexestrol.

Available in tablets containing 1 mg of the drug.

To be stored in a place protected from light observing safety precautions (List B).

SYGETHIN (Sygethinum)

Dipotassium salt of 3,4 bis (p sulfophenyl) hexane



White crystalline powder, soluble in water, sparingly soluble in alcohol. Aqueous solutions can be sterilized by the usual methods.

Has a weak estrogenic effect, intensifies uterine contractions and has a sedative influence on the gonadotropic function of the hypophysis cerebri.

Used in obstetric practice in uterine inertia, intrauterine asphyxia of the foetus and disturbances of the ovarian menstrual cycle.

As a labour accelerating agent, sygethin is injected subcutaneously or intramuscularly in a dose of 1–2 ml 2% solution. For a rapid effect it is administered intravenously. Can be used in combination with other labour accelerating agents.

In cases of intrauterine asphyxia of the foetus, the mother is given an intravenous injection of 2 ml 2% solution.

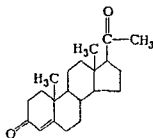
In disturbances of the menstrual cycle, sygethin is given orally in doses of 0.05–0.1 g.

Safety precautions are to be observed in storage (List B)

c) Hormones of the corpus luteum (gestagens) and their analogues

PROGESTERONE (Progesteronum)

4 Pregnene 3, 20 dione



Synonyms Agolutin Akrolutin, Corlutone Corpomone Geanestin, Gestrol, Gestone, Glanducorpin, Gynlutin, Lipolutin, Lucorten, Luteine, Luteogan, Luteopur, Luteostab, Luteosterone, Lutocyclin, Lutolform, Lutogyl, Lutren, Lutromon, Lutrone, Macrogestin, Neolutin, Progelan, Progesteroid, Progestin, Progeston, Progestonaq, Proluton, Syngestrone

White crystalline powder, insoluble in water, soluble in alcohol, ether, chloroform and fats. Melting point 127—129°

Progesterone is the hormone of the corpus luteum for medical purposes it is prepared synthetically

Progesterone brings about the transition of the mucous membrane of the uterus from the proliferative phase caused by the follicular hormone to the secretory phase, after fertilization it promotes the transition of the endometrium to the condition necessary for the development of the fertilized ovum. It also diminishes the excitability and contractility of the muscles of the uterus and tubes and stimulates the development of the terminal elements of the mammary glands

Used in pathological processes associated with insufficiency of the corpus luteum: dysfunctional uterine bleeding, functional and anatomical insufficiency of the genital organs, painful menstruation (algomenorrhea) due to underdevelopment of the genital organs, habitual and threatened abortion, sterility (after the preliminary administration of estrogenic preparations). It has also been reported that progesterone is effective in the treatment of late toxicosis of the second half of pregnancy

Administered intramuscularly or subcutaneously in the form of oil solutions

In bleeding associated with dysfunction of the ovaries, progesterone is administered (after curettage of the uterus) for 6—8 days in a daily dose of 0.005 g (5 mg). If it is impossible to carry out curettage, progesterone is administered even during bleeding. When progesterone is given while bleeding continues, the latter may be temporarily intensified (for 3—5 days), it is advisable to give preliminary blood transfusions (200—250 ml) to patients who have lost much blood. When bleeding has stopped treatment should not be discontinued for at least 6 days. If bleeding does not stop after 6—8 days further administration of progesterone is not advisable (S. K. Lesnoi)

In hypogenitalism and amenorrhea treatment is begun with estrogenic preparations with the aim of causing sufficient proliferation of the endometrium, immediately after stopping the administration of estrogens, injections of progesterone are begun, 5 mg daily for 6—8 days (see Folliculin, Hexestrol, Diethylstilbestrol)

In algomenorrhea (dysmenorrhea) progesterone not infrequently abates or overcomes the pain. Treatment is begun 6—8 days before menstruation. Progesterone is administered in daily injections of 3—5 mg for 4—6 days. The course of treatment can be repeated several times. In algomenorrhea associated with

Administered intramuscularly in the form of a 0.6% oil solution. Doses are individualized depending on the peculiarities of the case and the effectiveness of treatment. Usually one injection of 12 mg (2 ml solution, 21 000 units) is given per week, course of treatment — 2—3 injections. The effect of the first injection is usually manifested on the 3rd—6th day.

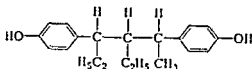
Contraindications and possible complications when using diethylstilbestrol dimethyl ether are the same as when using other synthetic analogues of folliculin.

Available in ampoules containing 2 ml 0.6% oil solution (12 mg dimestrol per ampoule).

To be stored in a place protected from light, observing safety precautions (List B).

OCTESTROL (Octoestrolum)

3 Ethyl 2,4 bis (p hydroxyphenyl) hexane



Synonyms: Benzeztrolum, Octofololin

White crystalline powder, practically insoluble in water, freely soluble in alcohol and vegetable oils. Melting point 160—162°.

Octestrol is a synthetic drug which, like hexestrol, has a pronounced estrogenic action when taken orally. Similar to hexestrol in potency, 1 mg represents 10 000 units of activity.

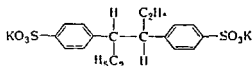
Indications, contraindications and doses are the same as for hexestrol.

Available in tablets containing 1 mg of the drug.

To be stored in a place protected from light, observing safety precautions (List B).

SYGETHIN (Sygethinum)

Dipotassium salt of 3,4 bis (p sulfophenyl) hexane



White crystalline powder, soluble in water, sparingly soluble in alcohol. Aqueous solutions can be sterilized by the usual methods.

Has a weak estrogenic effect, intensifies uterine contractions and has a sedative influence on the gonadotropic function of the hypophysis cerebri.

Used in obstetric practice in uterine inertia, intrauterine asphyxia of the foetus and disturbances of the ovarian menstrual cycle.

As a labour accelerating agent, sygethin is injected subcutaneously or intramuscularly in a dose of 1—2 ml 2% solution. For a rapid effect it is administered intravenously. Can be used in combination with other labour accelerating agents.

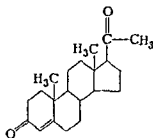
In cases of intrauterine asphyxia of the foetus, the mother is given an intravenous injection of 2 ml 2% solution.

In disturbances of the menstrual cycle sygethin is given orally in doses of 0.05—0.1 g.

Safety precautions are to be observed in storage (List B)

c) Hormones of the corpus luteum (gestagens) and their analogues
PROGESTERONE (Progesteronum)

4 Pregnene 3, 20 dione



Synonyms Agolutin, Akrolutin, Corlutone, Corpomone, Geaneslin, Gestrol, Gestone, Glanducorpin, Gynlutin, Lipolutin, Lucorten, Luteine, Luteogan, Luteopur, Luteostab, Luteosterone, Lutocycin, Lutoform, Lutogyl, Lutren, Lutromon, Lutrone, Macrogestin, Neolutin, Progelan, Progesteroid, Progestin, Progeston, Progestonaq, Proluton, Syngestron

White crystalline powder, insoluble in water, soluble in alcohol, ether, chloroform and fats. Melting point 127—129°

Progesterone is the hormone of the corpus luteum for medical purposes it is prepared synthetically

Progesterone brings about the transition of the mucous membrane of the uterus from the proliferative phase caused by the follicular hormone to the secretory phase, after fertilization it promotes the transition of the endometrium to the condition necessary for the development of the fertilized ovum. It also diminishes the excitability and contractility of the muscles of the uterus and tubes and stimulates the development of the terminal elements of the mammary glands.

Used in pathological processes associated with insufficiency of the corpus luteum: dysfunctional uterine bleeding, functional and anatomical insufficiency of the genital organs, painful menstruation (algomenorrhea) due to underdevelopment of the genital organs, habitual and threatened abortion, sterility (after the preliminary administration of estrogenic preparations). It has also been reported that progesterone is effective in the treatment of late toxemia of the second half of pregnancy.

Administered intramuscularly or subcutaneously in the form of oil solutions.

In bleeding associated with dysfunction of the ovaries, progesterone is administered (after curettage of the uterus) for 6—8 days in a daily dose of 0.005 g (5 mg). If it is impossible to carry out curettage, progesterone is administered even during bleeding. When progesterone is given while bleeding continues the latter may be temporarily intensified (for 3—5 days), it is advisable to give preliminary blood transfusions (200—250 ml) to patients who have lost much blood. When bleeding has stopped treatment should not be discontinued for at least 6 days. If bleeding does not stop after 6—8 days further administration of progesterone is not advisable (S. K. Lesnoi).

In hypogonadism and amenorrhea treatment is begun with estrogenic preparations with the aim of causing sufficient proliferation of the endometrium immediately after stopping the administration of estrogens, injections of progesterone are begun, 5 mg daily for 6—8 days (see Folliculin, Hexestrol, Diethylstilbestrol).

In algomenorrhea (dysmenorrhea) progesterone not infrequently abates or overcomes the pain. Treatment is begun 6—8 days before menstruation. Progesterone is administered in daily injections of 3—5 mg for 4—6 days. The course of treatment can be repeated several times. In algomenorrhea associated with

underdevelopment of the uterus treatment with progesterone can be combined with the administration of estrogenic preparations Estrogens are administered at the rate of 10 000 units each second day for 2—3 weeks progesterone is then given for 6 days

In habitual and threatened abortion administration of progesterone should be started as soon as possible and continued till the 4th month of pregnancy, As a preventive measure injections of 0.005 g (5 mg) are given each second day during the first 4 months of pregnancy In threatened abortion the same dose is given every day If symptoms of incipient abortion should appear the dose of progesterone is increased to 10 mg daily During the second half of pregnancy progesterone is prescribed in a dose of 5—10 mg per day if there should be untimely labour like uterine contractions (threat of premature labour) Progesterone should not be given after the 37th week of pregnancy The total amount of progesterone for the course of treatment should not exceed 0.3—0.35 g

Maximal single and daily dose intramuscularly, for adults 0.01 g (2 ml 0.5% oil solution)

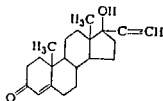
Available in ampoules containing 1 ml 0.5% oil solution (5 mg progesterone)

To be stored in well closed bottles or sealed ampoules in a place protected from light observing safety precautions (List B)

Rp Sol Progesteroni oleosae 0.5% 10
D t d N 6 in amp
S 1 ml intramuscularly

PREGNIN (Pregnenin)

Δ^4 17 Ethynylandrosten 3 one 17 (β) ol or ethynyltestosterone



Synonyms Aethisteronum Ethisterone Gestone Oral Lutocycol Nalutron Oraluton Pranone Pregneninolone Pregnoral Progestoral Proluton C

White or slightly yellowish fine crystalline powder insoluble in water sparingly soluble in alcohol soluble in oils Melting point 268—274° Synthetic analogue of the corpus luteum hormone progesterone.

The biological and therapeutic action of pregnin is analogous to that of the natural hormone it is however only $\frac{1}{5}$ — $\frac{1}{6}$ as potent as progesterone A distinguishing feature of pregnin as compared with progesterone is the fact that its activity is maintained when taken orally especially when held under the tongue (absorption through the mucous membrane of the oral cavity)

Pregnin like progesterone is used in disturbances of the function of the ovaries associated with insufficiency of the corpus luteum In dysfunctional uterine bleeding pregnin (like progesterone) is administered in order to bring about the transition of the endometrium to the premenstrual condition which may lead to the stopping of bleeding Pregnin is also used in amenorrhea hypo oligomenorrhea and algomenorrhea In sterility pregnin (like progesterone) is prescribed after the preliminary administration of estrogenic preparations In habitual threatened or incipient abortion the use of progesterone is to be preferred

Pregnin is usually administered in a dose of 10 mg (two 5 mg tablets) 3 times a day

The length of treatment is the same as for the intramuscular administration of progesterone

Maximal doses for adults single—0.015 g, daily—0.05 g

When taking *pregnin* the tablet should be held under the tongue until completely dissolved so that the drug is absorbed and enters the body through the mucous membrane of the oral cavity. This method of administration promotes a better therapeutic effect than when the drug is absorbed from the stomach and intestine

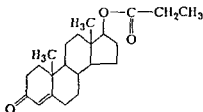
Available in tablets of 0.005 g (5 mg)

To be stored in a dry place protected from light, observing safety precautions (List B)

F. Preparations of the male sex hormones (androgens) and their synthetic analogues

TESTOSTERONE PROPIONATE (*Testosteronum propionicum* *Testosteroni propionas*)

Δ^4 Androsten-3-one-17(β)-ol-17 propionate



Synonyms: Agovirin, Androfort, Androlin, Andronate, Andrusol P, Anerlan, Homosteron, Malestron, Neohombreol, Oreton F, Perandren, Sterandryl, Synandrone, Testolutin, Testoviron, Viormone

White or slightly cream coloured crystalline powder, soluble in vegetable oils, freely soluble in alcohol and ether, insoluble in water. Melting point 118–123°

Testosterone is the male sex hormone (androgen), it is produced in the male sex glands and is necessary for the formation of the genital organs and the development of the secondary sexual characteristics of the male. The constant production of testosterone begins at sexual maturation and continues till the period of waning sexual activity.

In medical practice, synthetic testosterone propionate is used; it has all the biological and therapeutic properties of the natural hormone but is more slowly absorbed and is more stable in the body. Testosterone propionate is administered parenterally, it is ineffective when given orally since it is destroyed quite rapidly in the liver.

Besides its specific androgenic effect, testosterone, like other androgens, influences other functions and systems of the body, among other things it has an active influence on nitrogen and phosphorus metabolism. It has a marked anabolic action and promotes the assimilation of proteins by the tissues, especially the muscles.

Use in males: sexual underdevelopment, functional derangements in the genital system, male climacteric and associated vascular and nervous disorders, acromegaly.

In some cases the administration of testosterone propionate gives a beneficial effect in hypertrophy of the prostate, improvement in the general condition, abatement of urination disorders, etc.

In women the administration of testosterone propionate or other androgens inhibits the gonadotropic function of the pituitary body suppresses the function of the follicular apparatus of the ovaries causes atrophy of the endometrium and suppresses the function of the mammary glands. Testosterone propionate is sometimes administered to women for therapeutic purposes in climacteric vascular and nervous disorders (in cases when folliculin and other estrogenic preparations are contraindicated (tumours of the genital organs and mammary glands and uterine bleeding). It is also used simultaneously with ray therapy in cancer of the mammary glands and ovaries. In women of advanced age testosterone propionate can be used in dysfunctional uterine bleeding.

Testosterone propionate can also have a favourable effect in early stages of hypertensive disease and in angineuritic forms of stenocardia (M. S. Vovsi and M. I. Shevlyagina).

In all cases the drug is only used in accordance with a physician's prescription; during treatment the patient must be kept under careful observation.

Testosterone propionate is administered in the form of intramuscular injections of oil solutions.

Dosage for males in cases of eunuchoidism and congenital underdevelopment of the gonads or removal of the gonads surgically or as a consequence of trauma as well as in acromegaly: 0.025 g (25 mg) daily or 0.05 g (50 mg) each second or third day. The length of treatment depends on the effectiveness of therapy and the character of the disease. Usually treatment is continued for a lengthy period of time. After an improvement in the clinical picture has been achieved maintenance doses are given 0.005–0.01 g daily or each second day.

In impotency associated with functional insufficiency of the sex glands, fatigue or nervous exhaustion as well as in the male climacteric accompanied by vascular and nervous disorders 10 mg is administered daily or 25 mg 2–3 times a week over a period of 1–2 months.

In the initial stage of hypertrophy of the prostate 10 mg is given each second day for 1–2 months.

In dysfunctional uterine bleeding in women about 50 years old or more injections of 1 ml 2.5% solution (25 mg) are given each second day 20–30 injections in all. The bleeding should first be stopped by curettage of the uterus and the mucous membrane removed should be examined in order to exclude the possibility of there being a malignant process in the uterus. The administration of androgens to young women is not expedient (S. K. Lesnoi).

In vascular and nervous disorders of climacteric etiology when the use of folliculin and its analogues is contraindicated testosterone propionate is administered in a dose of 10 mg each second day for several weeks. The use of methyltestosterone is preferable in such cases.

A beneficial effect is obtained in some cases in the treatment of angina pectoris when testosterone is given in a dose of 10–12.5 mg once a week. If the drug is tolerated well the number of injections is increased to twice a week (over a period of 3–5 weeks). Toward the end of treatment the dose and number of injections are again reduced. The course of treatment consists of 15–20 injections. It is an advantage simultaneously to administer diethylstilbestrol in a dose of 0.5 mg. The beneficial effect is due to the improvement in the blood circulation and processes of metabolism in the myocardium; there are also favourable changes in respect to the lipids of the blood: an elevation of the lecithin (cholesterol coefficient) (L. G. Fomina). The best effect is observed in angineuritic forms of stenocardia. In pronounced *cardiosclerosis* hormone treatment is only slightly effective: the use of hormones may even lead to insufficiency of the myocardium (M. S. Vovsi).

In the treatment of patients with cancer of the ovaries and mammary glands testosterone propionate is administered from the beginning of the post-operative period in a daily dose of 0.05 g (50 mg) for 100 days (F. M. Lampert). The dose is then lowered to 0.3, 0.25 or 0.2 g (6, 5 or 4 ml 5% solution).

per week for a month during the next 2 months 0.15 g (3 ml) is given per week and then 0.1 g (2 ml) per week for 2 months. After that maintenance doses are prescribed for a lengthy period. Testosterone propionate is administered to women up to 60 years old (estrogenic preparations are prescribed for women over 60 years old). When using large doses of testosterone propionate the patient's condition must be kept under careful observation; large doses may cause retention of water and salts in the body. In women, the voice may become lower in pitch and there may be an excess growth of hair on the face and body along with puffy edema of the face. Sexual excitability may be increased and there may be vertigo and nausea.

Overdosage of the drug in dysmenorrhea may lead to the stopping of menstruation.

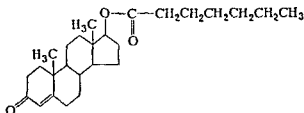
Maximal doses: single and daily, intramuscularly 0.05 g.

Available in ampoules containing 1 ml 1%, 2.5% and 5% oil solution (0.01, 0.025 and 0.05 g testosterone propionate).

To be stored in sealed ampoules in a place protected from light, observing safety precautions (List B).

TESTOSTERONE ENANTHATE

Δ^4 Androsten-3-one-17-ol enanthate



White or slightly yellowish crystalline powder, soluble in vegetable oils, ether and alcohol, insoluble in water. Melting point 36–37.5°.

Has a somewhat stronger and more lasting androgenic effect than testosterone propionate.

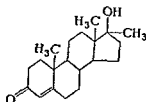
Used in males in cases of underdevelopment of the genital organs and secondary sexual characteristics, and in disturbances of sexual function (early climacteric).

Administered intramuscularly in a dose of 1 ml 5% oil solution (0.05 g) once or twice a week.

Available in ampoules containing 1 ml 5% oil solution.

METHYLTESTOSTERONE (Methyltestosteronum)

17 α Methyl Δ^4 androsten-3-one-17-ol



Synonyms: Agovirin Dragees, Andrometh, Androl, Anerlan perlingual, Glosso Sterandryl, Hormale, Malogen, Masenone, Melandren, Neo hombraol (M), Oraviron, Orelon (M), Stenendiol, Testoral, Viormone oral.

White or slightly cream coloured fine crystalline powder odourless and tasteless soluble in alcohol ether and acetone insoluble in water sparingly soluble in vegetable oils Melting point 161—167°

Methyltestosterone is a synthetic analogue of testosterone It has the biological and therapeutic properties of the natural hormone like testosterone it stimulates the development of the male genital organs and secondary sexual characteristics

Methyltestosterone is not destroyed by the enzymes of the gastrointestinal tract and maintains its activity when taken orally For a greater effect however it is recommended that methyltestosterone should not be swallowed but that the tablet should be held under the tongue until completely dissolved

Methyltestosterone is a very potent androgen but it is less active than testosterone propionate when absorbed through the mucous membrane of the mouth it has approximately $\frac{1}{2}$ — $\frac{1}{4}$ the potency of testosterone propionate administered intramuscularly

If there are indications for intensive therapy with the male sex hormone injections of testosterone propionate are to be preferred

Methyltestosterone is prescribed for males in cases of sexual underdevelopment and functional sexual disturbances and in the male climacteric and associated vascular and nervous disorders

In primary eunuchoidism and hypogonadism due to congenital underdevelopment of the gonads as well as to their surgical removal (in tuberculosis or orchitis) or to trauma or injury through a pathological process methyltestosterone is administered in a daily dose of 0.03 g or more (up to 0.1 g) Large doses are usually prescribed the first 2—3 weeks and then as the sexual function improves the dose is reduced maintenance doses come to 0.025 g per day or 0.05 g each second day In moderate forms of hypogonadism doses of 0.02—0.025 g daily or each second day are sufficient Treatment is carried out for a lengthy period of time depending on the severity of the disease and the effectiveness of treatment In impotence arising from functional insufficiency of the sex glands fatigue or nervous exhaustion a daily dose of 0.01—0.02 g is administered In the male climacteric accompanied by vascular and nervous disturbances 0.005—0.015 g is administered daily for 1—2 months in the initial stage of hypertrophy of the prostate due to age 0.02—0.03 g is given daily for 1—2 months treatment is repeated depending on the course of the process In cancer of the prostate methyltestosterone is contraindicated

In delayed sexual development infantilism and lardy growth in male children and juveniles methyltestosterone is prescribed in a dose of 0.005—0.01 g per day the length of treatment depends on the effect achieved

Methyltestosterone is sometimes prescribed in a dose of 0.005—0.015 g per day as a tonic for convalescents after acute infections, trauma and surgical operations as well as in cases of early waning of sexual vigor in advancing age etc. this use is partially due to the anabolic action of the drug In such cases however methylandrosterone is to be preferred as it has a weaker androgenic effect

Methyltestosterone is likewise used in the treatment of stenocardia Doses are individualized ranging from 0.01—0.02 g once a week to 0.01 g daily or each second day (see Testosterone propionate)

Methyltestosterone is prescribed for women in cases of functional uterine bleeding during the climacteric and preclimacteric periods In a dose of 0.015 g (three 5 mg tablets to be held under the tongue) 3—4 times a day over a period of 40—50 days (after preliminary curettage of the mucous membrane of the uterus see Testosterone propionate) 2.4—3 g methyltestosterone is used for the course

In climacteric vascular and nervous disorders in women methyltestosterone is used when the administration of estrogenic preparations is contraindicated The dose is 0.005 g 1—3 times a day and administration is continued until the disorders disappear if necessary the drug is again prescribed in the same dose

In dysmenorrhea (algotmenorrhea) in women of advanced age, the drug is administered in a dosage of 0.01—0.02 g per day for 5—6 days preceding menstruation

In cancer of the ovaries and mammary glands and in chorioepithelioma prescribed in a dosage of 0.05—0.1 g per day prior to and for a lengthy period after the operation, used in the same doses in cases of metastasis, sometimes alternating with injections of testosterone propionate or combining methyltestosterone treatment with ray therapy

Maximal doses for adults single—0.05 g daily—0.1 g

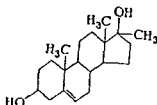
When administered to women for too long, general masculinization is possible lowering of the pitch of the voice, hirsutism of the masculine type heightening of the sexual libido, etc. Overdosage of the drug in dysmenorrhea may lead to the stopping of menstruation

Available in tablets of 0.005 g (5 mg)

To be stored in a place protected from light observing safety precautions (List B)

METHYLANDROSTENDIOL (Methylandrostandiolum, Methandriolum)

17 α Methyl Δ^5 androsten 3 β ,17 β diol



Synonyms Andriodiol, Anormon Diolostene Masdiol, Mestendiol Metandiol, Metandriol, Methostan Neosteron Notandron Protandren Stenedrol Stenediol, Testodiol, Troformone.

White crystalline substance insoluble in water sparingly soluble in alcohol Melting point 202—206°

Methylandrostandiol is closely related to methyltestosterone in chemical structure, it is also similar in biological properties but its androgenic activity is considerably less while the anabolic effect is relatively strong. Consequently it can be used in disturbances of protein metabolism while the androgenic (masculinizing) effect is relatively weak

Used in order to intensify protein anabolism in convalescents after severe trauma and operations and infectious and other diseases, likewise used in osteoporosis, tardy growth malnutrition etc

Since methylandrostandiol has only a slight androgenic effect it can be used to heighten anabolism in females

Because of the moderate androgenic and antiestrogenic effect the drug can also be administered to women in cases requiring a lowering of the activity of the follicular hormone (during the climacteric and in functional dysmenorrhea as well as in cancer of the mammary gland)

Doses must be individualized. Usually adults are prescribed 0.025—0.05 g per day, and children — 0.01—0.025 g. Administered in the form of tablets to be held under the tongue till completely dissolved. Protein rich food is prescribed simultaneously. In osteoporosis administered in a dosage of 0.05—0.1 g per day gradually reducing the dose to 0.025—0.05 g per day. In climacteric disorders and dysmenorrhea prescribed in a dosage of 0.025—0.05 g per day. In cancer of the mammary gland — 0.1 g or more daily, subsequently reducing the dose to 0.05—0.075 g

Treatment with methylandrostandiol should be carried out under the observation of a physician

When the drug is taken for lengthy periods there may be excessive growth of hair on the face and trunk and the skin may become more greasy
Available in tablets of 0.01 and 0.025 g to be held under the tongue
To be stored in a dry place protected from light observing safety precautions

G Gonadotropic hormones

CHORIONIC GONADOTROPIN

Gonadotropins are substances which stimulate the development and function of the sex glands (male and female). They include the gonadotropic hormone of the anterior lobe of the pituitary the gonadotropic hormone extracted from the serum of the pregnant mare and chorionic gonadotropin extracted from human pregnancy urine.

The biological action of chorionic gonadotropin is similar to that of luteinizing hormone of the anterior pituitary. In the female it stimulates the formation ripening and rupture of the follicle and the transformation of the corpus luteum and heightening of its function it also prolongs the life of the corpus luteum.

In the male the administration of chorionic gonadotropin stimulates the function of the interstitial cells of the testes and normalizes testicular development in delayed puberty.

The preparation is available in lyophilic form solutions are unstable and are therefore prepared *ex tempore*.

The potency of chorionic gonadotropin is determined biologically and is expressed in units of activity. One unit equals 0.1 mg of standardized powder.

Preparations of chorionic gonadotropin are put out abroad under the names Antélobine Entromone Follutein Gonabion etc.

Chorionic gonadotropin is used in insufficiency or disturbances of the sexual function both in females and males. In females in absence or disturbance of the menstrual cycle due to hypophysial insufficiency sterility of hypophysial ovarian etiology and functional uterine bleeding in males in cryptorchidism and delayed puberty due to hypofunction of the hypophysis.

Chorionic gonadotropin solution is administered intramuscularly. In cases of anovulatory cycle in women the preparation is prescribed from the middle of the cycle 3—5 injections of 1000—1500 units. Courses of treatment are repeated during several cycles.

In profuse and frequent menstruation chorionic gonadotropin is prescribed in order to prolong the existence of the corpus luteum doses of 1000—2000 units are given for 4—5 days preceding expected menstruation.

In other indications doses range from 500 to 1500 or 2000 units per injection depending on the character and severity of the disease.

In cryptorchidism in males the hormone is administered in doses of 500 units 2—3 injections per week for 6—8 weeks the course of treatment is repeated if necessary in 3—4 weeks.

If treatment is unsuccessful there are grounds for suspecting mechanical obstruction requiring surgical intervention.

In delayed puberty the preparation is given 2—3 times a week in a dosage of 1000—1500 units the course of treatment is repeated if necessary.

Children are given smaller doses—100 200 or 500 units per injection.

Chorionic gonadotropin is available in ampoules containing 500 and 1000 units ampoules containing solvent are supplied. Before use the ampoule of gonadotropin is opened and the solvent added by means of a syringe the solution is drawn back into the syringe in order to make the injection.

To be stored in sealed ampoules at a maximum temperature of 20° in a place protected from light.

V. DRUGS INHIBITING THE FUNCTION OF THE THYROID GLAND

METHYLTHIOURACIL (Methylthiouracilum)

6 Methyl 2 thiouracil



Synonyms Alkiron, Antibason, Methiacil, Methicil, Methiocil, Methiuracil, Melyrin, Muracil, Orcanon, Prostrumyl, Strumacil, Thumecil, Thiomidil, Thiothyron, Thioryl, Thyril, Thyrobasine, Tiotiron

White or slightly yellowish crystalline powder bitter taste freely soluble in solutions of ammonia and alkalis, sparingly soluble in water, alcohol and ether

Methylthiouracil is a synthetic antithyroid (thyrostatic), like other substances of this group it causes a lessening of thyroxine synthesis by the thyroid gland, thanks to which it has a specific therapeutic effect in hyperthyroidism. Like other antithyroids, it also causes a lowering of basal metabolism.

The antithyroid action of methylthiouracil is due to acceleration of the withdrawal of iodides from the thyroid, and lowering of the activity of the enzyme systems concerned in the oxidation of iodides to iodine which leads to inhibition of the iodizing of thyroglobulin and delay in the conversion of diiodo tyrosine into thyroxine. Besides this disturbance of thyroxine synthesis may depend on the reaction of methylthiouracil with the free iodine formed in the thyroid from iodides.

Along with its antithyroid effect, methylthiouracil causes hyperemia, hyperplasia and hypertrophy of the thyroid (so called strumogenic effect) this reaction is secondary and is due to heightening of the thyrotropic function of the hypophysis.

Methylthiouracil is used in the treatment of exophthalmic goiter and thyrotoxicosis of various degrees.

Administered orally. Doses range from 0.25 g 3 times a day to 0.05 g twice a day, depending on the course of the disease. Treatment is begun with large doses, which are gradually reduced. Usually when treating severe and moderate thyrotoxicosis a dose of 0.25 g is given 3 times a day the first 10 days, 0.25 g twice a day the next 10 days and from then on 0.25 g or less (0.1–0.2 g) once a day for several months. In moderate thyrotoxicosis, smaller doses are sufficient—0.2 g and less the first few days, subsequently reducing the dose.

Maximal doses for adults single—0.3 g, daily—0.75 g.

When preparing patients with thyrotoxicosis for an operation, treatment with methylthiouracil is carried out in the dosage indicated above, until a marked abatement of thyrotoxicosis symptoms and an improvement in the general condition have been achieved, after which methylthiouracil is withdrawn for 10–15 days before the operation, prescribing instead iodine preparations (Lugol's solution 5–10 drops twice a day) or diiodotyrosine, in order to lessen hyperemia and tendency of the glandular tissue to hemorrhage at the time of the operation. Mercapozolil is a more convenient antithyroid for preparing patients for such operations.

Side effects may occur when using methylthiouracil and consequently treatment should be carried out under the careful observation of a physician. Because of the possibility of leukopenia, neutropenia and agranulocytosis, a careful watch must be kept on the blood picture and a white blood count should

be made at least 2—3 times a month and the leukocyte formula examined. When changes are detected in the blood the drug must be immediately withdrawn and leukopoietic stimulants (nucleic acid thesian etc.) folic acid and vitamin B₁₂ prescribed. The drug is also withdrawn on the appearance of urticaria, dermal pruritus, nausea, pain in the joints and elevated temperature.

In order to prevent a strumogenic effect iodine is given simultaneously in microdoses or 0.05 g diiodotyrosine once or twice a day.

Methylthiouracil is contraindicated in nodular forms of thyrotoxic goiter and leukopenia as well as in thyrotoxicosis during the second half of pregnancy. Methylthiouracil should not be given in combination with other drugs capable of causing leukopenia (aminopyrine and its analogues, sulfanilamides etc.).

Available in powder form and in tablets of 0.25 g.

To be stored in well closed bottles in a place protected from light observing safety precautions (List B).

MERCAZOLIL (Mercazolilum)

1 Methyl 2 mercaptoimidazole



Synonyms: Antiroid, Basolan, Danantizol, Favistan, Mercazole, Methimazole, Methothylin, Tapazole, Thiamazole, Thycapzol.

White or light brown powder, bitter taste, freely soluble in water and alcohol, sparingly soluble in ether. Melting point 142—144°.

Mercaptoimidazole is a very potent antithyroid. It is similar to methylthiouracil in the character of its action but has a more pronounced antithyroid effect, lowers basal metabolism to a greater degree and at the same time has a weaker strumogenic effect.

Used in exophthalmic goiter and thyrotoxicosis of various degrees. Administered orally after meals. The dosage depends on the severity of thyrotoxicosis symptoms. In mild and moderate forms of thyrotoxicosis prescribed in a dose of 0.005 g 2—3 times a day; in severe forms 0.005 g 3—4 times a day. The daily dose is subsequently lowered depending on the effect, 0.005 g being given 2—3 times a day. Administration of the drug is continued for a lengthy period after the disappearance of thyrotoxic symptoms (up to several months), doses of 0.0025—0.005 g being given daily or 2—3 times a week until a persistent therapeutic effect has been achieved. If treatment is discontinued too soon a relapse of the disease is possible.

Mercaptoimidazole can also be used in preparing patients for operation on account of thyrotoxicosis; unlike methylthiouracil it does not cause hyperemia and tenderness of the thyroid to hemorrhage.

Mercaptoimidazole is usually tolerated well in therapeutic doses but treatment should nevertheless be carried out under the observation of a physician; blood examinations are necessary 2—3 times a month since in isolated cases patients may develop leukopenia, nausea, skin rash and pain in the joints are also possible. If side effects develop the dose is reduced or the drug withdrawn. 10% calcium chloride solution or calcium gluconate is given orally.

Contraindications are the same as for methylthiouracil.

Available in tablets of 0.005 g.

To be stored in a dry place protected from light observing safety precautions (List B).

POTASSIUM PERCHLORATE (Kalium perchloricum) KClO₄

White crystalline substance, odourless, sparingly soluble in water, insoluble in alcohol.

Potassium perchlorate is an antithyroid (thyrostatic) substance. The thyrostatic effect is due to a lowering of the thyroid's ability to accumulate iodine which leads to decreased formation of thyrotoxin. Potassium perchlorate has a weaker strumogenic effect than methylthiouracil.

Chiefly used in mild and moderate forms of thyrotoxicosis of short duration accompanied by considerable malnutrition. In severe forms especially in patients who have previously received large amounts of other thyrostatic drugs, treatment with potassium perchlorate is less effective.

Administered orally before meals. The dosage and length of treatment are fixed individually depending on the patient's condition, the severity of the disease, the effectiveness of treatment and tolerance for the drug.

In light forms of thyrotoxicosis, the daily dose during the first 4–6 weeks of treatment is usually 0.5–0.75 g (0.25 g 2–3 times a day) and then 0.25 g per day. The course of treatment is for 2–4 months. The total amount of drug for the course is from 50 to 70 g.

In moderate form of thyrotoxicosis 0.75–1 g is administered daily (0.25 g 3–4 times a day) over a period of 4–6 weeks. The dose is then reduced to 0.25–0.5 g per day. The length of treatment is 4–5 months making a total of 70–100 g of the drug for the course.

In severe forms, 1 g potassium perchlorate daily is prescribed for 6–8 weeks, after which the dose is lowered to 0.25–0.5 g per day. Length of treatment 5–7 months. Total drug for the course — 100–130 g.

In order to prevent a relapse, treatment is discontinued only when there have been no symptoms of thyrotoxicosis for 1½–2 months.

Potassium perchlorate is usually tolerated well. In 3–4 weeks after the beginning of treatment an abatement of nervous and mental excitement is noted along with improved sleep and appetite, abatement of tachycardia, disappearance of tremor in the hands, sweating and other manifestations of thyrotoxicosis, there is a considerable gain in weight. In exophthalmic forms of thyrotoxicosis even small doses of the drug cause a lessening of exophthalmos.

The drug is not suitable for preparing patients for an operation on the thyroid, since a lengthy period of time is necessary for an antithyroid effect, besides which there may be a heightened tendency of the gland to hemorrhage.

When using potassium perchlorate, there may be headache, loss of appetite, nausea and other dyspeptic symptoms, in such cases the dose should be reduced or the drug withdrawn.

In respect to the blood there may be slight leukopenia and thrombopenia the first few days, the leukocyte formula then returns to the initial condition.

Treatment with potassium perchlorate should be carried out under a physician's observation.

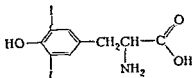
Contraindicated in pregnancy and ulcer of the stomach and duodenum.

Available in powder form and in tablets of 0.25 g.

To be stored under ordinary conditions, observing safety precautions (List B).

DIIODOTYROSINE (Diiodotyrosinum)

3,5 Diiodo 4 hydroxyphenylalanine



Synonyms Agontan, Apothyrin, Dityrin, Jodglobin, Jodgorgon.
White crystalline powder, sparingly soluble in water. Contains about 55% organic iodine.

Diiodotyrosine is an amino acid formed in the thyroid through the iodization of tyrosine. Subsequently diiodotyrosine is converted into thyroxine. Diiodotyrosine has no marked hormonal action but it inhibits the production of the thyrotropic hormone of the anterior lobe of the hypophysis which activates the thyroid gland.

For medical use the drug is prepared synthetically.

Diiodotyrosine is used in conjunction with methylthiouracil and other antithyroid drugs in order to lessen the strumogenic effect and also in mild and moderate forms of hyperthyroidism. Administered orally 0.05 g 2–3 times a day in cycles of 20 days with breaks of 10–20 days in treatment.

Maximal doses for adults: single—0.075 g daily—0.2 g.

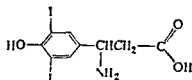
Diiodotyrosine is not prescribed in secondary hyperthyroidism arising during the use of iodine preparations.

Available in tablets containing 0.05 g diiodotyrosine.

To be stored in well closed bottles or tubes in a cool dry place protected from light.

BETASIN (Betasinum)

β (3,5-Diiodo-4-hydroxyphenyl) β alanine



White crystalline powder, sparingly soluble in water. Prepared synthetically. Differs from diiodotyrosine in the position of the amino group in the side chain.

Analogous to diiodotyrosine in action and indications for use.

Administered orally in a dose of 0.05 g 2–3 times a day.

Available in tablets of 0.05 g.

To be stored in well closed bottles in a cool dry place protected from light.

VI ENZYME PREPARATIONS

PANCREATIN (Pancreatinum)

Enzyme preparation from the pancreas of cattle. Fine amorphous yellowish powder with characteristic odour of dried animal tissue, sparingly soluble in water, insoluble in alcohol and other solvents.

Contains the principal enzymes of the pancreas, chiefly trypsin and amylase. Standardized by the biological method. 1 g contains 25 units.

Use: achylia, pancreatitis and digestive disorders associated with diseases of the liver and pancreas, anacid and hypoacid gastritis, chronic enterocolitis.

Administered in a dosage of 0.5–1 g 3–4 times a day before meals, to be drunk down with a glass of Borzhomi mineral water or with a solution of sodium bicarbonate.

Children are prescribed doses of 0.1–0.5 g.

Available in powder form and in tablets of 0.5 g.

To be stored in glass bottles or well closed cardboard boxes in a cool dry place.

PEPSIN (Pepsinum)

Preparation containing a proteolytic enzyme. Obtained from the mucous membrane of the stomach of swine, weakened by the addition of lactose.

White or slightly yellowish powder, sourish sweet taste, faint characteristic odour, soluble in water and 20% alcohol.

Used in digestive disorders (usually in conjunction with dilute hydrochloric acid) achylia hypo and anacid gastritis dyspepsia etc

Administered orally in a dose of 0.2—0.5 g 2—3 times a day before or during meals in powders or in 1—3% solution in dilute hydrochloric acid children are given doses of 0.05—0.5 g

Available in powder form

To be stored in well stoppered bottles in a cool place protected from light

ACIDIN PEPSIN (Acidin pepsinum)

Analogous preparations *Acidol pepsin* *Acipepsol* *Betacid* *Pepsacid* etc

Tablets containing 1 part pepsin to 4 parts of betaine hydrochloride When introduced into the stomach betaine hydrochloride is easily hydrolyzed with the formation of free hydrochloric acid 0.4 g betaine hydrochloride corresponds to approximately 16 drops of dilute hydrochloric acid

Used in hypo and anacid gastritis achylia and dyspepsia

Dose for adults one 0.5 g tablet 3—4 times a day

Dose for children from $\frac{1}{4}$ 0.25 g tablet to $\frac{1}{2}$ 0.5 g tablet 3—4 times a day depending on the age

Tablets are dissolved in $\frac{1}{4}$ to $\frac{1}{2}$ glass of water taken during or after meals

Available in tablets of 0.25 and 0.5 g

GASTRIC JUICE NATURAL (*Succus gastricus naturalis*)

Natural gastric juice obtained by I. P. Pavlov's method from healthy dogs and other domestic animals through a fistula in the stomach during simulated feeding

Colourless transparent liquid with acid taste and odour of chloroform (added as a preservative) Contains 0.5—0.52% free hydrochloric acid pH = 0.8—1.0

Administered orally in insufficiency of the gastric glands achylia hypo and anacid gastritis and dyspepsia

Administered to adults in a dose of 1—2 tablespoonfuls 2—3 times a day
Dose for children 2—5 years old — 1 teaspoonful or 1 dessertspoonful
6—12 years — 1 dessertspoonful or 1 tablespoonful

Available in bottles containing 100 and 150 ml

To be stored in a cool place protected from light

GASTRIC JUICE, ARTIFICIAL

Aqueous extract of the mucous membrane of the stomach of swine

Used as a substitute in cases of insufficient secretion of gastric juice Administered in a dose of 1 tablespoonful 2—3 times a day

Available in bottles of 100 and 250 ml

To be stored in a cool place protected from light

LYDASA

Preparation containing the enzyme *hyaluronidase* Obtained from bull testes

Analogous foreign preparations *Alidase* *Hyaluronidasum* *Hyalase* *Hyalidase* *Hyasa* *Hyason* *Hylase* *Invasinum* *Spredine* *Widase*

Light yellow or golden porous mass freely soluble in water

Hyaluronidase is an enzyme whose specific substrate is hyaluronic acid (see *Luronit*) The latter is a mucopolysaccharide whose molecule contains acetyl glucosamine and glucuronic acid Hyaluronic acid has high viscosity its biological significance consists chiefly in the fact that it is the "cementing" substance of connective tissue

Hyaluronidase or "spreading factor" depolymerizes hyaluronic acid and causes its depolymerization to glucosamine and glucuronic acid in this way lowering the viscosity It increases the permeability of the tissues and facilitates the movement of fluids in the inter tissue spaces

Hyaluronidase is contained in various tissues of the body The permeability of the tissues is regulated to a considerable degree by the relationship of the system "hyaluronic acid — *hyaluronidase* The antiphlogistic effect of various

medicinal agents (salicylates pyrazolone derivatives ACTH cortisone etc.) is due to a considerable extent to their ability to reduce the activity of hyaluronidase. On the contrary the action of some substances which cause greater permeability (for example, bee and snake poison) is partially due to their containing hyaluronidase.

The action of hyaluronidase is reversible. When its concentration is lowered the viscosity of the hyaluronic acid is restored. It follows that hyaluronidase can be used for temporarily lowering the viscosity of hyaluronic acid.

Preparations containing hyaluronidase (lydasa and ronidasa) are now obtained from bull testes.

Lydasa is a specially purified preparation suitable for parenteral administration. It is administered subcutaneously in contractures (hip and shoulder joints) cicatrices after burns and operations, Dupuytren's contractures, spondylitis ankylopoietica and hematomas (N. N. Priorov et al.). Good results have been reported in the treatment of diffuse forms of scleroderma (V. A. Rakhmanov and R. Kh. Khmelitsky). Lydasa is also employed in order to accelerate the absorption of medicines when administered subcutaneously (isotonic solutions, contrast mediums, etc.).

Available in ampoules containing 0.1 g sterile dry substance. The contents of the ampoule are dissolved in 1 ml sterile 0.5% procaine hydrochloride solution and injected near the affected area, either under the skin or under the scar tissue. Injections are given every day or each second day. Course of treatment, 10 or 15 injections. The therapeutic effect is manifested in a softening of cicatrices, the appearance of mobility in joints, the elimination or lessening of contractures and the resolution of hematomas; the effect is more pronounced in the initial stages of the pathological process. In the presence of indications it is an advantage to give injections of lydasa in conjunction with therapeutic gymnastics.

Allergic skin reactions sometimes occur during treatment.

Contraindications: malignant neoplasms, tuberculosis and other infectious diseases and inflammatory processes.

To be stored in sealed ampoules at room temperature in a place protected from light.

RONIDASA

Hyaluronidase preparation for external application.

Obtained from bull testes. Fine light yellow powder.

Use: treatment of cicatrices (burn postoperative keloid, etc. — chiefly of recent origin), Dupuytren's contractures (initial stages), contractures and impaired mobility of the joints after inflammatory processes and traumas with extravasation into the soft tissues, preparation for plastic skin operations on account of scarring, contractions, chronic tendovaginitis, persistently non-healing wounds.

Ronidasa powder is applied to a gauze napkin folded 4 or 5 times and moistened with sterile isotonic saline; the gauze is then placed on the affected area, covered with wax paper and fixed in position with a soft bandage. The amount of ronidasa used depends on the extent of the affected area and comes to 0.5 g or more per application. The dressing can be left for 16–18 hrs. On drying it is again moistened and the same amount of ronidasa is added. The preparation is applied daily for 15–60 days. When used over a lengthy period a 3–4 day break in treatment is made every fortnight. When treating a persistently non-healing wound the gauze is moistened with isotonic saline containing 10,000–20,000 units of penicillin per ml. Aseptic conditions must be ensured. In contractures treatment with the preparation is combined with the therapeutic gymnastics.

The preparation is tolerated well; in rare cases irritation of the skin may occur, but this quickly passes away when a short break is made in treatment.

Contraindications are the same as for lydasa.

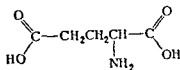
Available in hermetically sealed vials containing 5 g of the preparation
To be stored at room temperature in a place protected from light

VII AMINO ACIDS AND PROTEIN HYDROLYSATES

A Amino acids

GLUTAMIC ACID (*Acidum glutamicum*)

(+) Glutamic acid or α aminoglutaric acid



Synonyms Acidogen Acidulin Glutaminic acid Glutan Glutansin

White crystalline powder acid taste sparingly soluble in cold water freely soluble in hot water and solutions of alkalis and acids insoluble in alcohol

Glutamic acid is concerned in the process of nitrogen metabolism in the body In reactions of metabolism most of the nitrogen of the majority of amino acids passes through the stage of conversion to glutamic or aspartic acid or to α alanine During the process of metabolism glutamic acid is continuously formed from other amino acids

Glutamic acid assists in rendering ammonia innocuous Ammonia unites with glutamic acid to form glutamine which is harmless for the body the excretion of ammonia through the kidneys in the form of ammonium salts is also intensified

Considerable amounts of glutamic acid are contained in the proteins of the grey and white substances of the brain and spinal cord it is concerned in protein and carbohydrate metabolism and stimulates oxidizing processes Binding ammonia and rendering it innocuous is of importance for the normal functioning of the central nervous system Glutamic acid also assists in the synthesis of acetylcholine and adenosine triphosphoric acid and in the transportation of potassium ions As part of the protein component of the myofibrils it plays an important role in the activity of the skeletal musculature

In medical practice glutamic acid is mostly used in treating diseases of the central nervous system schizophrenia epilepsy (chiefly mild attacks with equivalents) psychoses (somatogenic, intoxication involuntional) reactive conditions proceeding with symptoms of exhaustion depression and other mental and nervous diseases In psychiatry the drug is used in delayed mental development of diverse etiology Down's disease and acute and restorative stages of poliomyelitis Favourable results have likewise been reported in the treatment of patients with progressive muscular dystrophy glutamic acid being used in combination with pachycarpine or glycine The administration of glutamic acid is also recommended for preventing and overcoming neurotoxic symptoms which may arise when using isoniazid and other drugs of the isonicotinic acid hydrazide group (see also p 352) According to contemporary findings the antitoxic effect of glutamic acid in these cases depends not only on the binding of ammonia and formation of nontoxic glutamine but also on the formation of isonicotinic acid hydrazone with the α ketoglutaric acid which is formed when glutamic acid is desaminized in the body

Glutamic acid is usually administered orally less often intravenously Adults are usually given 1 g crystalline glutamic acid 2-3 times a day Children are given the following doses up to 6 months old - 0.3-0.5 g daily from

6 months to 1 year—0.5–0.9 g from 1 to 3 years—1–1.5 g over 3 years—2 g (in 2–4 administrations) The drug is taken 15–30 min before meals if dyspeptic symptoms develop it is taken during or after meals The course of treatment is from 1–2 to 6–12 months

The drug can also be given orally in the form of a paste containing 5% glutamic acid 93% invert sugar and 2% water as well as in the form of a 1% solution in 25% glucose solution

For intravenous administration glutamic acid is available in ampoules in the form of a 1% solution Doses for adults 10–20 ml per day or each second day Doses for children up to 3 years old—2 ml from 3 to 5 years—3 ml from 5 to 10 years—5 ml over 10 years—10 ml A total of 15–20 injections are given For the first injection children are given 1–2 ml less than the dose indicated

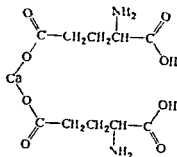
Side effects vomiting watery stool excitement of the central nervous system Quickly pass away when the dose is lowered At times when glutamic acid is given over a lengthy period a lowering of the hemoglobin content as well as leukopenia may occur

Contraindications feverish conditions diseases of the liver kidneys and gastrointestinal tract diseases of the hemopoietic organs heightened excitability violent psychotic reactions

When taking glutamic acid orally it is advisable after the dose to clean the teeth and rinse the mouth with a weak solution of sodium bicarbonate During treatment the urine and blood must be examined regularly

Glutamic acid is to be stored in glass bottles in a place protected from light

Calcium glutamate



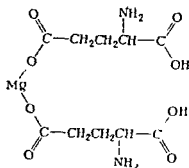
White powder of bitter taste soluble in water Solutions are sterilized by holding at 100° for 30 min

Use mental disorders associated with cerebral atherosclerosis post traumatic epilepsy senile psychoses tuberculous meningitis (acute stage and treatment of sequelae) acute stage of arachnoencephalitis and poliomyelitis Also used in reactive conditions and psychoses (on a par with glutamic acid)

Administered orally in the form of a 10% solution Dose for adults 20–50 ml 3 times a day Doses for children up to 3 years old—5 ml from 3 to 5 years—10 ml from 5 to 10 years—15 ml over 10 years—20–30 ml 3 times a day Administered over a period of 4–6 months if necessary the course of treatment can be repeated in 2–3 months

Administered intravenously to adults in a dose of 10 ml 10% solution daily or each second day (first injection not to exceed 3–5 ml) Doses for children up to 3 years old—2 ml from 3 to 5 years—3 ml from 5 to 10 years—5 ml over 10 years—10 ml (first injection 1–2 ml less than indicated doses) Course of treatment 15–20 injections

Magnesium glutamate

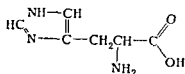


Used in the form of a 10% solution in mild forms of epilepsy, psychic equivalents, neurotic reactions, involutional psychoses and hypertonic, antispastic and cerebral crises

Methods of administration and doses are the same as for calcium glutamate

HISTIDINE (Histidinum)

α Amino β imidazolepropionic acid



Synonyms Gerulcin, Heruchin, Herulcin, Laristin, Larostidin, Stellidin

Histidine is an essential amino acid. It is contained in various organs and is a component of carnosine—a nitrogenous extractive substance of muscles. Histidine undergoes decarboxylation in the body, with the formation of histamine (see p. 132).

In medical practice histidine hydrochloride has found application in the treatment of ulcer of the stomach and duodenum, and hepatitis. The mechanism of the therapeutic action is not clear.

Administered intramuscularly in a dose of 5 ml 4% solution every day for 25–30 days. In order to prevent relapse, 5–6 injections are given every 2–3 months.

Available in ampoules containing 5 ml 4% solution of histidine hydrochloride.

To be stored in a place protected from light.

Rp Sol Histidin 4% 50

D t d N 10 in amp

S 5 ml intramuscularly daily

LEUCINE (Leucinum)

A mixture of amino acids has been approved for use under the name of "Leucine". Composition: leucine 3%, glutamic acid 0.5%, glycine 3%, glucose 10%, sorbose 5%, sodium chloride 1%, water to make 100%.

Colourless transparent liquid, sterilized by holding at 100° for 30 min.

Use: disturbances of carbohydrate metabolism, diseases of the liver accompanied by reduced secretion of bile, anemia, toxicosis, muscular dystrophy, sequelae of poliomyelitis, neuritis, mental diseases.

Administered orally. Adults: 20–30 ml 3 times a day. Children: 1 teaspoonful, 1 dessertspoonful or 1 tablespoonful, depending on the age, also 3 times a

day Course of treatment 1—1½ months Intravenously adults are given injections of 10—20 ml each second day (no more than 5 ml for 1st injection) Children 5 7 or 10 ml (no more than 3—5 ml for 1st injection) The course of treatment consists of 15—20 injections

Contraindicated in diseases of the kidneys marked by the presence of albumin in the urine and blood diabetes mellitus and sclerosis of the cerebral vessels Should not be administered orally in cases of ulcer of the stomach and duodenum

Available in vials for oral administration and in ampoules of 10 and 20 ml

B Protein hydrolysates containing a mixture of amino acids

HYDROLYSIN (Hydrolysinum) (L 103)

Product of acid hydrolysis of bovine blood protein Light brown porous mass freely soluble in distilled water

Hydrolysin solution available ready for use is a transparent brown liquid with characteristic odour Contains about 1% total nitrogen 40—45% of this amount is nitrogen contained in free amino acids Hydrolysin solution contains 2% glucose and small amounts of sodium chloride and calcium chloride

Hydrolysin contains all the essential amino acids It has no antigenic properties making possible its administration to patients irrespective of the blood group parenteral administrations can be repeated irrespective of the intervals between them

Hydrolysin readily enters into protein metabolism It is easily assimilated by the body and can serve as a fully adequate source of protein for parenteral nutrition in various conditions accompanied by hypoproteinemia It also has a disintoxicating action

Principal indications 1) hypoproteinemia and malnutrition when parenteral protein nutrition is required including cases where the absorption of proteins is impaired as a consequence of diseases of the gastrointestinal tract 2) preparation of patients for major operations as well as parenteral nutrition in the postoperative period 3) sluggishly granulating wounds and suppurative processes 4) burns 5) intestinal obstruction 6) various other cases of disturbance of the protein balance in the body due to a diminished amount of proteins in the body or to heightened requirement for them (including radiation sickness) various intoxications

Hydrolysin can be administered intravenously intramuscularly or subcutaneously It is absorbed well when injected intramuscularly and subcutaneously When injected intravenously the patient's reaction must be carefully observed

Whatever the method of administration it should be dropwise beginning with 20 drops per min If there is good tolerance the rate may be increased to 40—60 drops per min Before injecting the solution is warmed to body temperature Up to 2 liters of solution may be administered at a time

In isolated cases side reactions may occur when hydrolysin is used nausea vomiting elevated temperature dermal pruritus and urticaria

Contraindications decompensated cardiac activity cerebral hemorrhage thrombophlebitis acute nephrosis and nephrosclerosis

Hydrolysin can be administered with isotonic saline glucose solution and blood in various proportions In order to improve the colloidal properties of hydrolysin native or dry human serum or plasma can be added at the rate of 10 ml of plasma per 100 ml of hydrolysin

Hydrolysin solution is available in ampoules and hermetically sealed bottles of 250—300 and 500 ml

The preparation can also be put out in dry form

To be stored at a temperature of 4—6°

TsOLIPK¹ PROTEIN HYDROLYSATE

Product of acid hydrolysis of the protein casein Available in the form of a solution—a transparent yellow liquid with a total nitrogen content of 0.7–0.75% On long standing a light flocculent precipitate may form but this readily goes into solution when shaken

Contains all the essential amino acids and is a fully adequate source of protein for parenteral administration

Indications and contraindications are the same as for hydrolysin

Administered subcutaneously and intravenously absorbed well when injected subcutaneously Administered dropwise 60–90 drops per min Up to 2 liters can be administered at a time Can also be used in combination with glucose solution blood or plasma substitute solutions

Available in ampoules of 250 ml

To be stored at ordinary temperature (14–20°)

AMINOPEPTID (Aminopeptidum)

Product of fermentative hydrolysis of bovine blood proteins

Available in the form of a solution ready for use—a transparent yellowish liquid pH = 6.4–6.7 Total nitrogen content 0.75%

Contains all the essential amino acids valuable preparation for parenteral protein nutrition Indications and contraindications are the same as for hydrolysin and TsOLIPK protein hydrolysate

Aminopeptid can be administered subcutaneously intramuscularly intravenously and rectally Subcutaneous and intramuscular injections are somewhat painful Intravenous administration is by the drip method beginning at a rate of 10–20 drops per min if tolerance is good the number of drops is increased to 50–60 per min If there should be side effects (a sensation of fever nausea difficult breathing etc) infusion is stopped for 5–7 min, after which it is renewed If side effects again develop administration is stopped or a shift made to subcutaneous or intramuscular injection Intramuscularly and subcutaneously injections are also begun at a rate of 10–20 drops per min subsequently going over to 50–60 drops per min If tenderness should develop from intramuscular or subcutaneous injections it is advisable to precede administration with an intramuscular or subcutaneous injection of 5–7 ml 0.5% procaine hydrochloride Aminopeptid can also be administered in the form of drip enemas (40–60 drops per min)

A total of 1–2 liters of aminopeptid can be administered in 24 hrs if necessary administrations can be repeated

Available in ampoules of 250 ml To be stored at ordinary temperature (14–20°)

VIII PLASMA SUBSTITUTES

A Heterogenous protein blood substitutes

THERAPEUTIC SERUM (LSB) prepared by N. G. Belenky's method

Protein preparation obtained from bovine blood specially processed to reduce the anaphylactogenic properties

Amber colour opalescent liquid Available in sterile form in ampoules of 50, 100 and 250 ml

Use prevention and treatment of shock (single dose of 250–1000 ml) acute and chronic hemorrhage (single dose of 100–250 ml) burns (up to 1000–2000 ml daily for several days until hematocrite values are normalized) peritonitis and intestinal obstruction (up to 1000 ml per day) sluggishly granulating wounds and protracted suppurative processes (single dose of 100–250 ml) various intoxications infections and other diseases

If shock is accompanied by great loss of blood blood transfusion must be given along with the administration of serum blood cannot be replaced by serum because the latter contains no erythrocytes

¹ Hematology and Blood Transfusion Institute

Serum can likewise be used as a medium for parenteral nutrition

Serum is administered in single doses and also repeatedly at intervals of not more than 5 days. Repeated administrations at more lengthy intervals are impermissible because of the anaphylactogenic properties of serum.

Because of its anaphylactogenic properties the transfusion of serum may give rise to a posttransfusion reaction.

When infusing serum intravenously a triple biological test must be made injecting 5, 10 and 15 ml at intervals of 3–5 min. If there is no reaction infusion can be continued. If there should be a reaction (hyperemia of the face, pain along the vein, transitory disturbances of respiration, etc.) infusion of the serum should be stopped without extracting the needle from the vein until the symptoms enumerated disappear and until measurement of the arterial pressure shows that it has not fallen. 1–5 ml serum is then injected into the vein. If no reaction develops transfusion of serum may be continued. If side effects again develop when this amount of serum is injected (i.e. 1–5 ml) or if there should be an onset of pain under the sternum, dyspnea, dry cough, headache, accelerated pulse, lowering of arterial pressure, etc. transfusion is immediately stopped and 20–40 ml 40% glucose solution injected intravenously, as well as 10 ml 0.5% procaine hydrochloride (inject slowly!) and 10 ml 10% calcium chloride solution. A subcutaneous injection of 1 ml 1% morphine is given and cardiovascular agents are prescribed as well as the inhalation of oxygen.

Transfusion of therapeutic serum is performed, as a rule, by the drip method at a rate not exceeding 30–40 drops per min. It is only when there are particular indications (shock, acute loss of blood and other cases where the rapid introduction of fluid is required) that the jet method is used. If tolerance is good 1–2 liters of serum can be given in a single administration.

Transfusion of therapeutic serum must be carried out with great caution, keeping the strictest watch on the patient's condition and determining the arterial pressure as well as the pulse before beginning transfusion. At the moment the biological test is made and during and after transfusion. The temperature must be measured and the urine and blood examined before transfusion and during the posttransfusion period the possibility of posttransfusion reactions must be borne in mind.

Transfusion of serum may be carried out independently or in combination with human plasma and blood, glucose and other blood substitute liquids.

Principal contraindications to the transfusion of serum: organic changes in the cardiovascular system with marked symptoms of decompensation, endocarditis, generalized thrombophlebitis, acute nephritis and nephrosclerosis, cerebral hemorrhage, cerebral confusion and concussion (acute stage), malignant neoplasms accompanied by break down of the tissues and ulceration, reaction during biological test.

Therapeutic serum can be administered rectally and by mouth.

Serum is administered rectally when intravenous transfusion is impossible in mental cases, etc. Rectal administration is contraindicated in organic affections of the rectum and sigmoid. The serum is introduced through a catheter at a depth of 30–40 cm (after a cleansing enema) at a rate of 60–70 drops per min. The serum is warmed to 30–35° for which purpose the end part of the rubber tube connected to the catheter is placed between two burners. The daily dose is 1–1.5 liters.

Therapeutic serum is prescribed by mouth in cases of protein dystrophy when intensified protein nutrition is required. Dose: 100–150 ml 2–4 times a day.

To be stored in sealed ampoules in a place protected from light at a temperature of 4–20°.

SERUM BK 8

Protein blood substitute BK 8 (proposed by V. A. Belitsker and K. I. Kalikova) is prepared from bovine serum. Transparent, light amber-coloured liquid, specific gravity 1.020–1.023, relative viscosity 1.4–1.6, pH = 7.4–7.8.

Available in sterile form in ampoules of 250 ml

The anaphylactogenic properties of the serum have been lowered considerably by special processing. Indications and contraindications are the same as for therapeutic serum prepared by N. G. Belyuk's method.

Serum BK 8 is administered intravenously (up to 2 liters at a time), subcutaneous administration is permissible. Serum may be given irrespective of the recipient's blood group.

Before each transfusion of BK 8 serum an individual compatibility test must be made: one or two drops of the preparation are mixed on a glass slide with a small drop of the patient's blood. Symptoms of agglutination are a contraindication to the use of the given batch of the preparation.

The body temperature must be measured and the blood and urine examined before transfusion of the serum and during the posttransfusion period.

When giving intravenous transfusions of serum, a triple biological test must be made, injecting successively 5, 10 and 15 ml at intervals of 3–5 min. If there is no reaction transfusion is continued. If there should be pain along the vein or a slight hyperemia of the face transfusion is stopped for 2–3 minutes, if the symptoms disappear transfusion is renewed. If a stronger reaction develops transfusion is stopped.

If there should be an onset of severe side effects (pain under the sternum, dry cough, lowering of the arterial pressure, etc.) transfusion is immediately stopped and the same measures are taken as in complications following the transfusion of donor blood, plasma and therapeutic serum (injections of glucose, procaine hydrochloride, etc.).

BK 8 serum is infused by the drip or jet method. Large doses (500 ml and more) are injected slowly.

To be kept in sealed ampoules in a place protected from light at a temperature of 2–10°.

B. Synthetic plasma substitutes

POLYGLUCIN (Polyglucinum)

6% colloidal solution (in isotonic saline) of a high molecular compound, a polymer of glucose obtained from water soluble dextran. The latter is synthesized from sucrose by the action of a certain strain of the microorganism *Leuconostoc mesenteroides*.

Analogous preparations: Dextran, Dextravan, Expandex, Gentran, Intradex, Macrodex, Plavolex.

Polyglucin is a transparent solution of a pale yellow tint, without odour. Thanks to the size of the molecule (the molecular weight is close to that of blood albumin), polyglucin does not penetrate through the vascular membranes and when introduced into the vascular bed circulates in it for a long time. Thanks to the high osmotic pressure, which is about 2½ times that of the proteins of blood plasma, polyglucin holds fluid within the vascular bed.

Polyglucin is a valuable plasma substitute: it quickly raises the arterial pressure in cases of acute loss of blood and maintains it at a high level for a lengthy period of time. It is not toxic and can be administered without regard to the blood group. It is partially excreted by the kidneys.

Used in operative, traumatic, posthemorrhagic and burn shock and acute loss of blood. Dose for one administration 200–1000 ml (up to 2 liters for one transfusion).

Infused by the drip method for the prevention of shock and for the treatment of mild forms. Administered by the jet method in cases of a considerable lowering of the arterial pressure (to below 80 mm Hg) in severe shock. 500–2,000 ml are injected. Patients who have lost much blood, as well as those with marked anemia are given a blood transfusion in addition (250–500 ml).

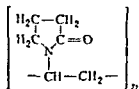
After infusing the first 25 ml of polyglucin administration is stopped for 2—3 min if there is no reaction transfusion is continued. If there should be complaints of constriction in the chest, difficulty in breathing and pain in the small of the back as well as the onset of a chill, cyanosis and impairment of circulation and respiration transfusion is stopped.

Contraindications to the transfusion of polyglucin: cranial trauma with heightened intracranial pressure (danger of raising the arterial pressure), cerebral hemorrhage, hypertensive disease, thromboembolism, diseases of the liver and kidneys, decompensated heart disease and other cases where the intravenous introduction of large amounts of fluid is contraindicated.

Available in sealed ampoules or hermetically closed bottles of 250 and 500 ml.

To be stored at room temperature.

POLYVINYLPIRROLIDONE (*Polyvinylpyrrolidonum*)



Polyvinylpyrrolidone (PVP) forms colloidal solutions with water. The large size of the PVP molecule ensures the preparation's lengthy circulation in the vascular bed. The most suitable preparations for plasma substitutes are those with a molecular weight not lower than 20 000, 25 000 and not higher than 40 000. If the molecular weight is below 20 000 the preparation is quickly excreted; if it is above 40 000 the preparation is retained in the body for a lengthy period.

3—5% solutions of PVP having a molecular weight of about 40 000 are used as a substitute for plasma. The intravenous infusion of such solutions causes a considerable increase in the plasma volume and raising of the arterial pressure which remains persistently at a high level.

The preparation has no antigenic properties; in rare cases a fixation reaction is observed, possibly due to an increase in the free histamine content in the tissues (freeing of bound histamine under the influence of the preparation) (see p. 132).

Polyvinylpyrrolidone is slowly excreted by the kidneys; part of the preparation administered is retained for a lengthy period in the reticuloendothelial cells of the spleen, in Kupfer's cells of the liver and in other organs.

3.5% PVP solution is used as a plasma substitute in traumatic and operative shock, acute loss of blood, burns and intestinal obstruction. Polyvinylpyrrolidone does not replace blood in cases of great loss of blood; administration of PVP should be combined with the transfusion of blood or erythrocytes.

Administered intravenously in a dose of up to 1 liter; if necessary infusions can be repeated.

Contraindications are the same as for polyglucin.

3.5% solution is available in ampoules of 250 and 500 ml; the solution is transparent and has a slight yellowish tint.

Polyvinylpyrrolidone is put out in foreign countries under various names: Kollidon (dry PVP preparation), Periston (2.5—3.5% PVP solution in physiological solution), Subtosan, Plasmosan (3.5% PVP solution in physiological solution containing sodium, potassium, calcium and magnesium salts), Plasdone, Vinisil, etc.

Solutions of polyvinylpyrrolidone of low molecular weight (12 000—18 000) in isotonic saline have also been proposed as disinfecting agents. When

introduced into the blood stream they bind toxins and are quickly excreted by the kidneys. Infused intravenously by the drip method in a dose of 100—500 ml. Indications: toxic forms of infectious diseases, burns (toxemia phase), intestinal obstruction, food poisoning, hepatic and uremic coma, etc.

Concentrated solutions of PVP (for example 25% subtosan solution) have been proposed as solvents for certain drugs (insulin, penicillin, hormones) in order to delay their absorption.

C Saline and colloidal-saline solutions

SODIUM CHLORIDE (*Natrium chloratum*, *Natrii chloridum*)

White cubic crystals or white crystalline powder, odourless, saline taste, freely soluble in water (1:3). Solutions are sterilized with running steam at a temperature of 100° for 30 min or by holding in an autoclave at a temperature of 120° for 15—20 min.

Sodium chloride is the principal component of saline and colloidal saline solutions used as plasma substitute fluids.

Sodium chloride is contained in the blood and in the tissue fluids of the body. The concentration in the blood is about 0.6%, its content ensures to a considerable extent the constant osmotic pressure of the blood.

Sodium chloride is ingested in sufficient amounts with the food. There may be deficiency of sodium chloride in the body in various pathological conditions accompanied by its increased excretion; if this is not compensated for by the introduction of sufficient amounts. There may be increased excretion during lengthy and pronounced diarrhea (e.g. in cholera), persistent vomiting, extensive burns with profuse exudation and hypofunction of the adrenal cortex.

When there is a deficiency of sodium chloride the blood is thickened due to water moving from the vascular bed into the tissues; if the deficiency is pronounced there may be spasms of the smooth muscles, convulsive contractions of the skeletal muscles and impairment of the function of the nervous system and the circulation.

Solutions of sodium chloride are classed as isotonic (or physiological) and hypertonic depending on the concentration. Isotonic solution has a concentration of 0.85%.

Isotonic saline is administered subcutaneously and intravenously as well as in enemas in cases of great losses of fluid and in intoxications (loss of blood, toxic dyspepsia, cholera, etc.).

It must be remembered that isotonic sodium chloride solution like other saline solutions containing sodium chloride quickly leaves the vascular system and only temporarily increases the volume of fluid circulating in the vessels; for that reason it is not sufficiently effective in cases of shock and great loss of blood. In such cases transfusions of blood plasma or plasma substitutes must be given simultaneously.

Isotonic saline has no irritating effect on the tissues; it is often used for washing wounds, the eyes and the mucous membrane of the nose. It is also used for dissolving various drugs and medicinal preparations.

Hypertonic solutions (3, 5 and 10%) are used externally in the form of compresses and washes in the treatment of suppurating wounds.

Because of the osmotic pressure compresses moistened with a hypertonic solution help to draw the pus from a wound. Hypertonic solutions also have a bactericidal effect. Hypertonic solution is injected intravenously (10—20 ml 10% solution) in pulmonary gastric and intestinal hemorrhage and also to increase uresis (osmotic diuresis). Sodium chloride enemas (75—100 ml 5% solution) are used to bring about defecation.

2—5% solution is administered orally and is used for stomach lavage in cases of poisoning with silver nitrate, the latter being converted into insoluble and nontoxic silver chloride

The subcutaneous injection of hypertonic solutions of sodium chloride is impermissible (necrosis of the tissues)

In treating Addison's disease, sodium chloride is used in addition to hormone preparations

Sodium chloride is also used for baths, lotions and gargles (1—2% solution in diseases of the upper respiratory passages)

Available in powder form and in tablets of 0.85 g.

RINGER—LOCKE SOLUTION (Solutio Ringer—Locke, Solutio Natrii chloridi composita)

Composition sodium chloride—9 g, sodium bicarbonate, calcium chloride and potassium chloride—0.2 g each, glucose—1 g, distilled water up to 1 liter Ringer—Locke tablets are also available with the salts in somewhat different proportion

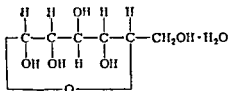
Ringer—Locke tablets

Composition sodium chloride—0.6 g, potassium chloride and calcium chloride—0.02 g each sodium bicarbonate—0.01 g glucose—0.1 g

In order to prepare Ringer—Locke solution 1 tablet is dissolved in 100 ml water

IX. SUGARS

GLUCOSE (Glucosa, Glucosum) Grape sugar



Synonyms Dextrosum Dextrose, Glycosum

Colourless crystals or fine white crystalline powder, odourless, sweet taste, freely soluble in water (1:5) sparingly soluble in alcohol For medical purposes isotonic solutions (4.5—5%) and hypertonic solutions (10—40%) are used

Solutions are sterilized by holding at 100° for 30 min 3 times or by holding once at 110° for 40 min Solutions are stabilized by the addition of 5 ml 0.1 N hydrochloric acid and 0.26 g sodium chloride per liter (10, 25 or 40% solution) before sterilization

Isotonic glucose solution is used for increasing the amount of fluid in the body and is at the same time a source of easily assimilated valuable nutritive matter The combustion of glucose in the tissues frees a considerable amount of energy, which is used for performing all the bodily functions

When injected into the vein, hypertonic solutions raise the osmotic pressure of the blood increase the movement of fluids from the tissues into the blood, intensify metabolic processes, improve the antitoxic function of the liver intensify myocardial contractions dilate the vessels and increase diuresis Glucose solutions are widely employed in medical practice in hypoglycemia, infectious diseases diseases of liver (hepatitis and dystrophy and atrophy of the liver), decompensated cardiac activity, pulmonary edema hemorrhagic diathesis toxic infections, various intoxications (poisoning with narcotics, hydrocyanic acid

or its salts, carbon monoxide, aniline arsine, phosgene and other substances), and other pathological conditions. They are used extensively in the treatment of shock and collapse and are one of the basic components of various blood substitutes and antishock fluids, they are likewise used for diluting cardiants, such as strophanthin, adonisid, convasid, erysimin, etc., before intravenous administration.

Isotonic solutions are administered subcutaneously (300—500 ml and more), intravenously (drip method) and in enemas (from 300—500 to 1000—2000 ml per day by the drip method).

Hypertonic solutions are administered intravenously 20, 40 or 50 ml per injection. When necessary they are infused by the drip method, up to 250—300 ml per day. In order to ensure more rapid and complete assimilation of glucose, insulin is sometimes given simultaneously (4—5 units subcutaneously). Glucose is often prescribed along with ascorbic acid.

Available in powder form, in tablets of 0.5 and 1 g, in ampoules containing 10, 20 and 50 ml 40% solution, as well as ampoules containing 10 ml 40% glucose solution with 1% ascorbic acid and ampoules containing 20 ml 25% glucose solution with 1% methylene blue. Solutions with methylene blue are used in cases of poisoning with hydrocyanic acid (see Methylene Blue).

To be stored in well closed bottles in a dry place, solutions are to be stored in sealed ampoules.

X. ALKALIS

MAGNESIUM OXIDE, calcined magnesia (Magnium oxydatum, Magnesium oxydatum, Magnesia usta)

MgO

Fine, white, light powder, practically insoluble in water. slowly dissolves in hydrochloric acid.

When introduced into the stomach magnesium oxide neutralizes the hydrochloric acid of the gastric contents with the formation of magnesium chloride, carbonic acid is not evolved. Consequently the antacid action of magnesium oxide is not accompanied by secondary hypersecretion. There are likewise no manifestations of alkalosis. As it moves into the intestine, magnesium chloride has a mild laxative effect.

Administered orally in doses of 0.1, 0.5 or 1 g in hyperacidity of the gastric juice, administered in doses of 3—5 g in cases of poisoning with acids, and as a mild laxative.

MAGNESIUM CARBONATE, BASIC, white magnesia (Magnium carbonicum basicum, Magnesium carbonicum basicum, Magnesia alba)

$MgCO_3 + Mg(OH)_2$

Light, white, easily pulverized lumps or white, fluffy powder, sparingly soluble in water, freely soluble in dilute acids.

Used externally as a dusting powder, and orally in hyperacidity of the gastric juice and as a mild laxative. Doses for adults 1—3 g 2—3 times a day, doses for children up to 1 year old—0.5—1 g, from 2 to 5 years—1—1.5 g, from 6 to 12 years—1.5—2 g.

CALCIUM CARBONATE, PRECIPITATED, precipitated chalk (Calcium carbonicum praecipitatum) $CaCO_3$

Fine, white crystalline powder, odourless and tasteless. insoluble in water, soluble in hydrochloric, nitric and acetic acid with the evolution of carbon dioxide.

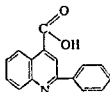
Administered orally in cases of hyperacidity of the gastric juice, in doses of 0.2—1 g 2—3 times a day.

An ingredient of tooth powders.

XI. DRUGS WHICH PROMOTE THE EXCRETION OF SALTS

CINCHOPHEN (Cinchophenum)

2 Phenylcinchoninic acid, 2 phenylquinoline 4 carboxylic acid



Synonyms Aciphen, Aciphenochinolinum, Agophen, Agotan, Artexin, Artiphphan, Atocin, Atophan, Cinchophan, Cinophen, Ikterosan, Interphan, Pheno phan, Phenoquin, Quinophan, Tervalon, Tophosan, Urosol, Usal, Vantyl, Vio phan

Yellowish crystalline powder, insoluble in water, sparingly soluble in dilute acids, freely soluble in dilute solutions of caustic alkalis and sodium carbonate, sparingly soluble in alcohol. Melting point 211–216°. Cinchophen promotes the movement of uric acid from the tissues into the blood, intensifies its excretion by the kidneys and increases the secretion of bile and gastric juice. Has an analgesic effect.

Used in gout. Administered orally in powders and tablets, in dosage of 0.25–0.5 g 3–4 times a day.

Maximum doses for adults single—0.5 g, daily—2 g.

When taking cinchophen it is advisable to drink large amounts of alkaline liquid (Borzhomi mineral water or a solution of sodium bicarbonate, 1 tea spoonful to a glass of water). Bicarbonates lessen the drug's irritating effect on the stomach and also assist in keeping the urates in the urine dissolved. When used over lengthy periods injuries to the liver and gastrointestinal tract are possible (icterus, atrophy of the liver, gastritis), as well as cystitis. In order to avoid complications it is recommended to administer the drug in cycles of 5 days with breaks of 1 week in treatment.

Contraindicated in diseases of the liver and kidneys, ulcer of the stomach, bronchial asthma and hay fever.

Available in powder form and in tablets of 0.5 g.

To be stored in a place protected from light, observing safety precautions (List B).

URODAN (Urodanum)

A mixture of the following composition: piperazine phosphate 25 parts, methenamine 8 parts, sodium benzoate 25 parts, lithium benzoate or citrate 2 parts, dibasic sodium phosphate 10 parts, sodium bicarbonate 37.5 parts, tartaric acid 37.5 parts.

Used in gout, biliary and urinary calculi, spondylarthritis, and chronic polyarthritis.

The use of urodan is based on reports in the literature that salts of piperazine and lithium form relatively soluble salts with uric acid and further its excretion. Changes in the acid-alkali balance may also be of significance.

Administered orally, 1 teaspoonful in $\frac{1}{2}$ glass of water 3–4 times a day before meals. Treatment is lengthy—30–40 days. If necessary the course can be repeated.

Urodan gives an effervescent solution when dissolved in water.

UROZIN (Urozinum)

Tablets containing 0.22 g piperazine phosphate, 0.1 g lithium benzoate and 0.25 g methenamine.

Used in place of urodan. Contains the main active substances of the latter. Indications for use are the same.

Administered orally 1—2 tablets with $\frac{1}{2}$ glass of water 3—4 times a day before meals Tablets should be pulverized before taking

HYPER SOL (Hypersolum)

A mixture of inorganic salts, in the form of a white powder, soluble in water Available in tablets of the following composition sodium bicarbonate 0.063 g, dibasic sodium phosphate 0.31 g, sodium chloride 0.782 g potassium chloride 0.055 g, sodium phosphate 0.069 g Proposed for the prevention and treatment of atherosclerosis

Administered orally 2 tablets twice a day before meals Tablets are dissolved in $\frac{1}{4}$ — $\frac{1}{2}$ glass of boiled water before taking

XII. CALCIUM AND POTASSIUM SALTS

CALCIUM CHLORIDE, CRYSTALLINE (Calcium chloratum crystallinum *Calcii chloridum crystallisatum*)



Colourless crystals or crystalline accretions odourless bitter saline taste very soluble in water (4:1) When dissolved there is a strong cooling effect Very hygroscopic, deliquescent in air Melts in its water of crystallization at 34° Contains 27% calcium Solutions are sterilized by holding at 100° for 30 min

Calcium is of very great importance for the body's vital activities Calcium ions are essential for the transmission of neural impulses, for contraction of the skeletal muscles and the myocardium, for the formation of bone tissue, for coagulation of the blood and for the normal activities of other organs and systems

Lowering the concentration of ionized calcium in the blood plasma causes tetany

Calcium chloride is used in medical practice in various pathological conditions a) insufficiency of the parathyroid glands accompanied by tetany or spasmophilia (see also Parathyroidin and Vitamin D), b) intensified excretion of calcium something that may occur when patients are immobilized for many months, c) allergic diseases (serum disease, urticaria angioneurotic edema, hay fever, etc.), as well as allergic complications following the administration of medicines (the mechanism of the antiallergic action is not clear, but it should be noted that the intravenous administration of calcium salts stimulates the sympathetic nervous system and increases the secretion of adrenalin by the adrenal glands) d) as an agent reducing vascular permeability, in hemorrhage vasculitis manifestations of radiation sickness, and inflammatory and exudative processes (pneumonia, pleuritis adnexitis, endometritis etc), e) skin diseases (pruritus eczema psoriasis, etc), f) parenchymatous hepatitis, toxic affections of the liver nephritis and eclampsia

Also used as a hemostatic in pulmonary, gastrointestinal, nasal and uterine hemorrhage In surgical practice sometimes administered before operations in order to increase the coagulability of the blood It should be noted however, that although calcium ions are essential for the process of coagulation, there is not sufficient reliable evidence of there being a hemostatic effect from calcium salts introduced into the body, the amount of calcium contained in the blood exceeds the amount necessary for the conversion of prothrombin into thrombin

Calcium chloride is likewise used as an antidote in poisoning with salts of magnesium (see Magnesium sulphate, p 37), oxalic acid and its soluble salts and soluble salts of hydrofluoric acid (formation of undissociated, nontoxic calcium oxalate and calcium fluoride)

Also used in conjunction with other methods and agents for the stimulation of labour

When administered orally (8–10 g) calcium chloride has a diuretic effect the mode of action is that of an acid forming diuretic (see Ammonium chloride)

Calcium chloride is administered orally a teaspoonful dessertspoonful or tablespoonful of 5–10% solution 2–3 times a day It is administered intravenously in doses of 5 10 or 15 ml 10% solution intravenous injections must be made slowly

In allergic diseases the use of calcium chloride in conjunction with anti histamines is recommended

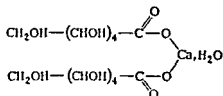
When administered intravenously there is a sensation of fever, first felt in the mouth and then spreading over the whole body This property of the drug is sometimes made use of in determining the speed with which the blood moves this is done by determining the time that elapses between intravenous injection and the appearance of a sensation of fever

Calcium chloride solutions must not be injected subcutaneously since they cause marked irritation and necrosis of the tissues

Contraindicated in patients with a tendency to thrombosis in cases of advanced atherosclerosis and when there is a high concentration of calcium in the blood

Available in small glass bottles well stoppered and sealed with paraffin and in ampoules containing 5 and 10 ml 10% solution

CALCIUM GLUCONATE (Calcium gluconicum, Calcii gluconas)



White granular or amorphous powder odourless and tasteless sparingly soluble in cold water (1 50) freely soluble in boiling water (1 5) practically insoluble in alcohol and ether Contains 9% calcium Aqueous solutions for injection (10%) are prepared with boiling water and are sterilized by holding at 110° for 60 min Solutions are transparent and colourless pH = 6.0–7.5

Similar to calcium chloride in its principal pharmacological properties in indications and contraindications Causes less local irritation and is therefore suitable for subcutaneous and intramuscular injections

Administered orally intramuscularly and intravenously

Doses for oral administration adults—2–5 g or 1/2–1 teaspoonful 2–3 times a day before meals (or 2–6 or more 0.5 g tablets) children up to 2 years old—0.25–0.75 g from 2 to 5 years old—1 g from 6 to 12 years old—1.5 g (also 2–3 times a day)

For intramuscular and intravenous administration adults are prescribed 5–10 ml 10% solution daily or each second or third day depending on the indications Children are given 1–5 ml 10% solution each second or third day depending on the age Before administration the ampoule containing the solution is warmed to body temperature. It should be borne in mind that intramuscular administration may cause necrosis It is not advisable to give children intramuscular injections

Intravenous injections of calcium gluconate should be given slowly—over a period of 2–3 min The syringe should not contain any alcohol before being filled since alcohol precipitates calcium gluconate

When calcium gluconate is administered intravenously or intramuscularly side effects may occur in rare cases nausea vomiting diarrhea and retarded pulse These symptoms quickly pass away of themselves

the cardiac glycosides is partially due to their influence on the adenosine triphosphate — adenosinetriphosphatase system. Adenosine triphosphate is concerned in the transmission of neural impulses in the autonomic ganglia and improves transmission of neural stimuli from the vagus to the heart (V. V. Zakusov).

Adenosine triphosphate is available for medical use in ampoules containing 1% solution of the disodium salt and in the form of the monocalcium salt.

Disodium salt of adenosine triphosphate (Natrium adenosinum triphosphoricum) 1% neutral solution, prepared by neutralizing adenosine triphosphate with sodium hydroxide to pH=7.0. Transparent, colourless solution.

Use: muscular dystrophy and atrophy, dystrophic changes of the myocardium (with the simultaneous administration of cardiants), as well as spasms of the cardiac and peripheral vessels. It has been reported that adenosine triphosphate is effective in the treatment of infectious and other diseases of the nervous system (diencephalitis, diencephaloganglionitis, etc.), and motor disorders associated with parkinsonism, and also that it stimulates the uterine muscles and accelerates labour.

Administered intramuscularly. For course treatment, 1 ml 1% solution is given once a day the first 2—3 days and after that 1 ml twice a day or 2 ml once a day. The course of treatment consists of 30—40 injections. The course is repeated in 1—2 months, depending on the effect.

Adenosine triphosphate is not used in fresh myocardial infarction, or in inflammatory diseases of the lungs.

Available in powder form and in ampoules containing 1 ml 1% solution.

To be stored in a cool place (at a temperature of 4—5°).

Monocalcium salt of adenosine triphosphate (Calcium adenosinum triphosphoricum) White crystalline powder, odourless, soluble in water and in isotonic saline.

Available in ampoules containing 0.3 ml 10% solution in glycerine.

Before use ampoules are warmed in hot water and the contents diluted with 1 ml isotonic saline.

Administered subcutaneously and intramuscularly in a dose of 0.03 g (1 ampoule) once a day. The course consists of 30—40 injections.

MUSCLE-ADENYLIC PREPARATION (MAP)

Liquid obtained from brewer's yeast by biological synthesis (earlier prepared from muscular tissue), 1 liter contains up to 2 g adenilic acid (adenosine monophosphate). The preparation also contains fructose diphosphate and other biologically active acids. Approximates adenosine triphosphate in its mode of action. Causes dilation of the blood vessels and somewhat stimulates cardiac activity.

Chiefly used in myocardial dystrophy, stenocardia and spasms of the peripheral vessels (intermittent lameness, etc.).

Administered in a dose of 1 teaspoonful 2—3 times a day.

Available in vials of 50 ml.

To be stored in a cool place protected from light.

PHYTIN (Phytinum)

Complex organic phosphorus preparation containing a mixture of the calcium and magnesium salts of inositol phosphoric acids, for the most part inositol hexaphosphoric acid. Obtained from defatted hemp seed cake and other cakes. Contains 36% organic phosphate.

White amorphous powder, odourless, almost insoluble in water, soluble in 1 N hydrochloric acid (1:10).

Like other phosphorus preparations, stimulates hemopoiesis and intensifies the growth and development of bone tissue, improves nervous activity in diseases due to phosphorus deficiency. Use: various diseases of the nervous system, vascular hypotonia, hysteria, neurasthenia, impotence, malnutrition, rickets, osteomalacia, anemia, tuberculosis, diatheses, scrofulosis, etc.

Administered orally in powders, tablets and pills (often in combination with drugs containing arsenic and iron) in doses of 0.25–0.5 g 3 times a day over a period of 6–8 weeks. Daily doses for children up to 1 year old — 0.05–0.1 g, 2–5 years — 0.1–0.2 g, 5–12 years — 0.2–0.3 g.

Available in powder form and in tablets of 0.25 g.

PHYTOFERROLACTOL (Phytoferrolactolum)

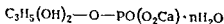
Tablets containing 0.2 g phytin and 0.2 g ferrous lactate.

Used in diseases associated with nervous exhaustion, anemia and general malnutrition.

Administered orally, 1 tablet 3 times a day.

CALCIUM GLYCEROPHOSPHATE (Calcium glycerophosphoricum)

Mixture of α and β isomers



White powder, odourless, slightly bitter taste, soluble in dilute hydrochloric acid, insoluble in alcohol and ether.

Used as a general tonic in malnutrition, overstrain, nervous exhaustion and rickets.

Administered orally. Adults are given 0.1–0.3 g 2–3 times a day, often in combination with drugs containing iron, arsenic and strychnine, children are given doses of 0.05–0.2 g.

Available in the form of granules in bottles of 100 g.

Glycerophosphate granules Composition: calcium glycerophosphate 10 parts, sodium glycerophosphate 2 parts, sugar 88 parts.

Used in the same way as calcium glycerophosphate.

Glycerophosphen (Glycerophosphenum) Tablets containing 0.2 g calcium glycerophosphate.

LECITHIN (Lecithinum)

Lecithins or choline phosphatides are esters of glycerol, one of whose hydroxyl groups is linked to phosphoric acid. The phosphoric acid in turn is linked with choline through an ester bond.

Lecithins are contained in various animal tissues and organs, there being an especially large amount in the brain matter, adrenals and erythrocytes. For medical use a preparation is available under the name of "Lecithin-cerebro", obtained from the brain of the ox by extraction.

Administered orally in nervous diseases, general prostration and anemia, in doses of 3–6 dragees a day.

Available in dragees containing 0.1 g lecithin.

To be stored in a dry place, protected from light.

LIPOCEREBRIN (Lipocerebrinum)

Prepared from the brain of cattle, contains phospholipid substances of brain tissue.

Used as a tonic in nervous exhaustion, neurosis, vascular hypotonia and overstrain.

Available in tablets of 0.5 g and ampoules of 1 ml for intramuscular injections. Lipocerebrin in ampoules is an aqueous suspension of lipid substances.

Oral doses — 1–2 tablets 3 times a day, intramuscular doses — 1 ml per day.

To be stored in well closed bottles in a cool, dry place.

PHOSPHREN (Phosphrenum)

Dragees containing organic phosphorus, lecithin, iron and calcium salts.

Used in general prostration, overstrain, neurasthenia and anemia. Prescribed in a dose of 2 tablets 2–3 times a day.

Available in dragées of 0.5 g.

XIV. DRUGS CONTAINING ARSENIC

SODIUM ARSENATE (*Natrium arsenicum*)

$\text{Na}_2\text{HAsO}_4 \cdot 7 \text{H}_2\text{O}$

Colourless crystals effloresces in air odourless soluble in water (1:17) almost insoluble in alcohol Aqueous solutions are alkaline they are sterilized by holding at 100° for 30 min

Used in the form of an aqueous solution for subcutaneous injections (often in combination with strychnine solution — see Duplex)

1% Sodium arsenate solution in ampoules (*Solutio natrii arsenici* 1% in amp) Transparent colourless liquid pH = 6.0–7.5

Administered as a general tonic in malnutrition and neuroses Because of its ability to stimulate to some extent the erythropoietic function of the bone marrow it is sometimes used in mild forms of anemia Also prescribed for the treatment of psoriasis

In large doses sodium arsenate like other inorganic arsenic containing drugs depresses leukopoiesis and is therefore used in the treatment of chronic myelogenous leukemia A solution of potassium arsenite is more often used for this purpose

1% sodium arsenate solution is injected subcutaneously In adults the initial dose is 0.2 ml once a day gradually raising the dose to 1 ml Before ending the course of treatment the dose is gradually reduced In cases of emaciation and anemia the number of injections for the course is 20–30 or infrequently 40 In psoriasis treatment is continued for 2–3 months

In leukemia 1–2 ml is injected per day for 4–6 weeks (the doses used exceed the maximal doses specified by the USSR State Pharmacopoeia) During treatment careful watch must be kept on the patient's condition if there should be side effects (nausea vomiting watery stool pigmentation of the skin) treatment is discontinued

Sodium arsenate and other inorganic arsenical drugs are contraindicated in affections of the kidneys neuritis marked anemia and dyspeptic disorders

Maximal doses for adults subcutaneously single—0.003 g daily—0.01 g

Maximal doses for children 2 years old single—0.0003 g daily—0.001 g 3–4 years single—0.0005 g daily—0.0015 g 5–6 years single—0.0005 g daily—0.0015 g 7–9 years single—0.001 g daily—0.003 g 10–14 years single—0.0015 g daily—0.0015 g Infants up to 2 years old are not prescribed sodium arsenate

To be kept locked (List A) in sealed ampoules in a place protected from light

DUPLEX

Aqueous solution of strychnine nitrate (0.1%) and sodium arsenate (1%), in ampoules of 1 ml Used as a general tonic in the same doses as 1% sodium arsenate solution

POTASSIUM ARSENITE SOLUTION Fowler's arsenical solution (*Liquor kali arsenicosi* *Liquor arsenicalis* *Fowleri* *Solutio kali arsenitis*)

Transparent colourless liquid with odour of camphor Contains 1% potassium arsenite

Administered orally in anemia emaciation neurasthenia and myasthenia in a dose of 1–3 drops 2–3 times a day

In cases of exacerbation of chronic leukemia without marked anemia or considerable enlargement of the spleen and lymph glands potassium arsenite solution is administered according to a schedule developed at the Central Hematology and Blood Transfusion Institute (A. A. Bagdasarov and M. S. Dultsin) beginning with 4–5 drops 3 times a day after meals adding 1 drop per dose each day When a dose of 9–10 drops is reached a 3 day break is made

in treatment After the interval, the patient receives the solution in the same dose in 4 day cycles with 3 day breaks in treatment In 3 weeks the dose is lowered to the initial amount, reducing the single doses 1 drop each day If there should be dyspeptic symptoms the drug is withdrawn

Doses of potassium arsenite solution used for the treatment of leukemia exceed the maximal doses specified in the USSR State Pharmacopoeia, during treatment a strict watch must be kept on the patient's condition and if there should be side effects treatment with the drug is immediately discontinued

Contraindications are the same as for sodium arsenate

Maximal doses for adults single—3 drops daily—10 drops

Maximal doses for children 2—4 years old, single—1 drop, daily—3 drops, 5—14 years, single—2 drops, daily—6 drops

Infants up to 2 years old are not prescribed potassium arsenite

To be kept locked (List A) in well stoppered bottles

ARSENIC ACID ANHYDRIDE (Acidum arsenicosum anhydricum, Arseni trioxydum) As_2O_3

Arsenic pentoxide, white arsenic

Heavy white porcelain like or glassy lumps of heavy white powder, dissolves very slowly in 65—80 parts of water, freely soluble in hydrochloric acid and solutions of caustic alkalis and carbonates of alkali metals

Applied externally as a necrotizing agent in skin diseases In stomatological practice used for necrotization of the pulp

Administered orally in pills in anemia, emaciation and neurasthenia, adults are given doses of 0.001 g, children are given less, depending on the age An ingredient of Arsenical Tablets and Blaud's Arsenic Tablets

Maximal doses for adults single—0.005 g, daily—0.015 g

Maximal doses for children 2 years old single—0.0002 g daily—0.0006 g, 3—4 years, single—0.0003 g, daily—0.001 g 5—6 years single—0.0005 g, daily—0.0015 g, 7—9 years, single—0.00075 g, daily—0.002 g, 10—14 years, single—0.001 g, daily—0.003 g Infants up to 2 years old are not prescribed arsenic acid anhydride

To be kept locked (List A) in well stoppered bottles

ARSENICAL TABLETS (Tabulettae Acidi arsenicosi obductae)

White sugar coated tablets (brownish yellow inside), each containing 0.001 g arsenic acid anhydride and 0.025 g black pepper

Administered in neurasthenia, emaciation and acute and chronic anemia in a dose of 1 tablet 2—3 times a day (for adults)

To be kept locked (List A)

BLAUD'S ARSENIC TABLETS (Tabulettae Blandi cum acido arsenicoso)

White sugar coated tablets (greenish brown inside), each containing 0.028 g ferrous sulphate and about 0.001 g arsenic acid anhydride

Administered in acute and chronic anemia emaciation and neurasthenia, 1 tablet 3 times a day (for adults)

To be kept locked (List A) in a dry place

XV. DRUGS CONTAINING IODINE

POTASSIUM IODIDE (Kalium iodatum, Kali iodidum) KI

Colourless or white cubic crystals or fine white crystalline powder, odourless bitter saline taste stable in dry air, deliquescent in moist air, very freely soluble in water (1:0.75), soluble in alcohol (1:12), freely soluble in glycerol (1:25)

Used as an iodine preparation in hyperthyrosis, endemic goiter, inflammatory diseases of the respiratory passages, ocular diseases (cataract, glaucoma etc) and bronchial asthma

Administered orally in solutions and mixtures in doses of 0.3–1 g 3–4 times a day. In pulmonary actinomycosis relatively large doses are given—1 tablespoonful of 10–20% solution 4 times a day. An ointment containing 15% potassium iodide has been proposed for epilation in fungus affections of the skin (M. M. Guseinov et al.).

It is not advisable to give intravenous injections of potassium iodide solutions because of the depressing effect of potassium ions on the heart. For the control of endemic goiter potassium iodide is added to table salt sold to the population of affected regions at a rate of 1–2.5 g per 100 kg.

To be stored in well stoppered bottles of amber glass.

Potassium iodide tablets, Antistrumlin (Antistrumlinum). Contain 0.001 g potassium iodide.

Used for the prevention of endemic goiter.

Administered in a dose of 1 tablet once a week in diffuse forms of goiter. The dosage is 1–2 tablets a day 2–3 times a week.

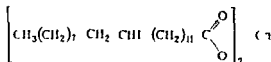
SODIUM IODIDE (Natrium Iodatum, Natrii Iodidum) NaI

White crystalline powder, odourless, saline taste, deliquescent in air, very freely soluble in water (1:0.05), freely soluble in alcohol (1:3) and in glycerol (1:2).

Indications for use and dosage are the same as for potassium iodide.

When intravenous administration of iodine preparations is necessary, as in cases of late syphilitic changes of the optic nerve and pulmonary actinomycosis, a 10% solution of sodium iodide is used, 5–10 ml for one infusion. Usually administered each second or third day, a total of 8–12 infusions.

CALCIUM IODOBENATE.



Synonym: Salodin.

Fine yellowish unctuous powder, odourless or with faint odour of fatty acid, insoluble in water, very sparingly soluble in alcohol and ether, freely soluble in warm dry chloroform. Contains 24% iodine and 4% calcium.

Used in cases where iodine therapy is indicated, especially in patients suffering from atherosclerosis, neurosyphilis, dry bronchitis and chronic rheumatism.

Administered orally in tablets, 0.5 g 1–3 times a day after meals (tablets should be thoroughly crumbled). After 2–3 weeks treatment a break of 2 weeks is advisable after which the course of treatment is repeated.

Contraindicated in severe decompensation of the cardiovascular system, diseases of the liver and kidneys and exophthalmic goiter.

Available in tablets of 0.5 g.

To be stored in tightly stoppered bottles of amber glass.

IOD HYPERSOL (Iod hypersolum).

Mixture of inorganic salts. Composition: sodium chloride 63.4 parts, potassium chloride 4.4 parts, anhydrous sodium sulphate 12.7 parts, acid sodium phosphate 6.3 parts, sodium bicarbonate 5 parts, sodium iodide 3.2 parts, sugar 5 parts.

White or slightly yellowish powder, freely soluble in water. Available in the form of granules.

It is assumed that administration of the preparation increases the reserve alkalinity of the blood, improves circulation and lowers the tone of the peripheral vessels.

Used for the prevention and treatment of atherosclerosis Administered orally, 0.5—1 g in $\frac{1}{4}$ glass cold water twice a day before meals

Contraindicated in pulmonary tuberculosis, malignant tumours and degeneration of the myocardium Symptoms of iodism may occur when taking the preparation irritation of the mucous membrane of the nose, respiratory passages, eyes, etc In such cases the preparation is taken after meals or the dose reduced Symptoms of iodism pass away when the preparation is temporarily withdrawn

XVI. DRUGS CONTAINING IRON

IRON, REDUCED (*Ferrum reductum*)

Fine, dark grey, dull powder, attracted by magnet when heated to incandescence is converted into black ferrosulfuric oxide soluble in dilute hydrochloric acid and in gastric juice

Iron is an important constituent of the body of man and animals It is an integral part of hemoglobin, myoglobin and various enzymes, as well as iron protein complexes found in the liver and spleen (ferritin, hemosiderin etc) Iron stimulates the function of the hemopoietic organs (see also Vitamin B₁₂, p 233)

When taken orally iron preparations are absorbed badly bivalent (ferrous) compounds are more readily absorbed and assimilated than trivalent (ferric) compounds For absorption to take place there must be a sufficient amount of free hydrochloric acid in the stomach for the solution and dissociation of the drugs, reducing agents, including ascorbic acid, serve to convert trivalent iron into bivalent, thus improving absorption The proteins of the mucous membrane of the stomach, as well as other proteins form complexes with iron in which form it is absorbed

Iron preparations are used for the treatment of hypochromic (iron deficiency) anemias of diverse etiology — posthemorrhagic, gastroenterogenic, symptomatic chloranemia chlorosis, etc When treating pernicious anemia with vitamin B₁₂ iron preparations are prescribed if the anemia becomes hypochromic (see pp 235 236)

Reduced iron is usually administered to adults in doses of 1 g 3—5 times a day immediately after meals Doses for children up to 1 year old — 0.01—0.1 g, from 5 to 6 years — 0.15—0.25 g, from 6 to 12 years — 0.3—0.5 g Course of treatment — at least 8—10 weeks In cases of secretorial insufficiency of the stomach gastric juice or dilute hydrochloric acid is taken simultaneously with iron The hydrochloric acid of the gastric juice is the principal factor ensuring solution and absorption of iron Absorption and assimilation of iron is improved if iron preparations are given in combination with ascorbic acid at the rate of 0.1—0.2 g for 1 g iron

The preparation is administered in the form of pills, capsules or wafers It is advisable to rinse the mouth thoroughly after taking iron since the teeth may become black after lengthy use, due to the formation of iron sulphide by reaction with hydrogen sulphide that may be present in the mouth (from carious teeth, etc)

Taking iron may lead to constipation

Available in powder form

To be stored in well stoppered moisture tight bottles

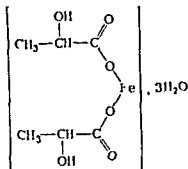
FERROHEMATOGEN (*Ferrohaematogenum*)

Preparation containing 11—12% reduced iron and dried blood of ox or swine

The presence of blood proteins improves the absorption of iron and heightens its effectiveness

To be taken in a dose of 1 tablet (0.3 or 0.5 g) 3—4 times a day

IRON LACTATE Ferrous lactate (Ferrum lacticum)



Greenish white crystalline powder or masses of fine needles characteristic odour. Slowly and sparingly dissolves in cold water (1:50), soluble in hot water (1:12), practically insoluble in alcohol, freely soluble in dilute mineral acids. Aqueous solutions are weakly acid and of greenish yellow colour, turning brown on contact with the air.

Iron lactate like other ferrous (bivalent) iron compounds is more easily absorbed from the gastrointestinal tract than ferric (trivalent) compounds. Iron lactate also causes no irritation of the mucous membranes.

Administered in hypochromic anemia in the form of powder or pills. Adults are given 1 g 3–5 times a day, children 0.1–1 g. When necessary gastric juice or dilute hydrochloric acid is prescribed simultaneously, ascorbic acid is also given.

Available in powder form.

To be stored in well stoppered bottles in a place protected from light.

HEMOSTIMULIN (Haemostimulinum)

Preparation of bovine blood with the addition of iron and copper salts.

Composition: dry hemalogen—25%, iron lactate—50%, copper sulphate—1%, glucose—20%. Light brown powder.

Used as an agent stimulating hemopoiesis in hypochromic anemia of diverse etiology.

Administered orally in powders or tablets. Adults 0.6 g 3 times a day during meals, children 0.1–0.5 g. To be drunk down with dilute hydrochloric acid, 10–15 drops to half a glass of water to be swallowed in small portions. Treatment is continued 3–5 weeks depending on the effect. Nausea sometimes occurs during administration of the preparation but this usually passes away of itself. It is not advisable to prescribe the preparation if there is diarrhea or vomiting.

Available in powder form and in tablets of 0.3 and 0.6 g.

To be stored in a cool place protected from light.

FERROUS CARBONATE WITH SUGAR (Ferrum carbonicum saccharatum, Ferrum carbonicum cum saccharo). Contains 10% ferrous iron. The sugar prevents the more active ferrous form from being converted into the ferric form.

Amorphous greenish grey powder of neutral reaction and sweet, slightly astringent taste. Carbon dioxide is evolved when dissolved in hydrochloric acid.

Indications for use are the same as for reduced iron. Doses for adults 0.3–0.5 g 3–4 times a day, doses for children correspondingly less. To be taken after meals.

To be stored in well stoppered bottles in a light place (to prevent the iron being converted into the ferric form).

The preparation is chemically not sufficiently stable; at present ferrous sulphate is mostly used instead of the carbonate.

FERROUS SULPHATE (*Ferrum sulfuricum oxydulatum, Ferrosi sulfas*)
 $\text{FeSO}_4 \cdot 7 \text{H}_2\text{O}$

Synonyms Iron vitriol, Copperas

Transparent blue green prismatic crystals or pale green crystalline powder, dissolves in 2.2 parts of water forming greenish solution of astringent taste and weakly acid reaction

Indications for use are the same as for reduced iron Doses are the same as for ferrous carbonate

Blaud's tablets (*dragées*) (*Tabletæ Blaudi*) — each contains 0.028 g ferrous sulphate Prescribed in a dose of 1 tablet 3—5 times a day

XVII. DRUGS CONTAINING COBALT

COAMID (*Coamidum*)

Coamid is a compound preparation of cobalt and nicotinamide (see p 230)

Lilac coloured powder, odourless, bitterish taste soluble in water (1:10), sparingly soluble in organic solvents Aqueous solutions are sterilized by the usual methods

Cobalt is an active stimulator of hemopoiesis, it promotes the assimilation of iron and stimulates processes of iron transformation (formation of protein complexes, synthesis of hemoglobin, etc)

Coamid has been proposed for the treatment of patients with hypochromic anemia, as well as Addison—Biermer's anemia and anemia associated with sprue

In iron deficiency anemias, iron preparations are prescribed simultaneously

Administered subcutaneously, 1 ml 1% aqueous solution per day The length of treatment depends on the course of the disease and the results obtained, the average course of treatment is 3—4 weeks

XVIII MISCELLANEOUS PREPARATIONS OBTAINED FROM ANIMAL BLOOD AND TISSUES

LURONIT (*Luronitum*)

Preparation obtained from the hyaloid body of the eye of the ox Contains hyaluronic acid (see Lydasa, p 283)

White powder with greyish tint, soluble in water with the formation of viscid solutions

Applied externally in the treatment of long healing wounds and ulcers with weak and sluggish granulation and retarded epithelization can be used for preparing granulating wounds and ulcers for plastic skin operations

Available in dry form in stoppered vials containing 0.1 g

Before use the contents of the vial are dissolved in 10 ml 0.5% procaine hydrochloride solution, on shaking a viscid solution is obtained which is spread evenly on the surface of a double layer gauze dressing This is applied to the wound and fixed in place with a bandage If necessary the contents of several vials are used The dressing is changed every 2 days

In treating wounds and ulcers the preparation is applied for 20—30 days, depending on the course of the process, when preparing for plastic skin surgery, it is used for 5—7 days

Contraindications a) acute inflammatory processes in the region of the wounds, b) diffuse necrosis of the tissues, c) superfluous granulation

HYALOID BODY

Preparation from the hyaloid body of the ox

Colourless, slightly opalescent liquid Proposed as an agent promoting the softening and resolution of scar tissue in extensive cicatrices from burns, operations and other causes and in contractures of the joints, as well as an analgetic in neuralgia, phantom limb syndrome and radiculitis Stimulates the formation of bone callus

Administered subcutaneously in a daily dose of 2 ml Length of treatment in neuralgia — 8—10 days In contractures and cicatrices — up to 25 days

Contraindications Infectious and acute inflammatory diseases general emaciation nephritis cirrhosis of the liver, cardiac insufficiency with edema malignant tumours

Available in ampoules of 2 ml The preparation is not used if it becomes turbid or a precipitate forms

PLASMOL (Plasmolum)

Preparation obtained from human blood Colourless slightly opalescent liquid odourless soluble in water

Used as a nonspecific desensitizing agent and analgetic in neuralgia neuritis radiculitis and other diseases of the peripheral nervous system accompanied by a pain syndrome as well as in ulcer of the stomach and duodenum bronchial asthma chronic inflammatory processes and arthritis

Administered subcutaneously 1 ml daily or each second day The course of treatment averages 10 injections Contraindicated in decompensated cardiac activity nephritis and endocarditis

Available in ampoules of 1 ml

To be stored in a cool place, protected from light

SPLENIN (Spleninum)

Nonprotein preparation obtained from the spleen of the ox

Transparent liquid with a slight yellowish tint saline taste and characteristic sharp odour preserved with 10% ethanol pH = 4.0—6.0

Splenin has been proposed for the prevention and treatment of early toxicosis of pregnancy Experimental findings show that the preparation normalizes changes in protein metabolism and heightens the disintoxicating function of the liver (V P Komissarenko)

Administered intramuscularly or subcutaneously

In I degree toxicosis of pregnancy 1 ml is injected each day for 8—10 days In II degree toxicosis 2 ml is administered daily for 10—13 days in either a single injection of 2 ml or 2 injections of 1 ml In unresponsive cases — 2 ml twice a day (morning and evening) In relapses of toxicosis the course of treatment is repeated

In III degree toxicosis 2 ml splenin is administered twice a day for 10—15 days

Simultaneously with the administration of splenin the intravenous injection of isotonic saline and 40% glucose solution is recommended as well as the prescription of bromides and other agents for the combined treatment of toxicosis of pregnancy In III degree toxicosis sufficient amounts of liquid must be introduced into the body

Available in ampoules of 1 ml To be stored in a place protected from light

HEMATOGEN (Haematogenum)

Preparation obtained from the defibrinized blood of cattle

Used in anemia and malnutrition

Administered orally Adults are given 1 tablespoonful or 0.5—1 g 2—3 times a day children from $\frac{1}{2}$ teaspoonful to 1 dessertspoonful

Available in bottles of 250 ml

HEMATOGEN CHILDREN'S

Composition dry blood 2.5 g per cake ascorbic acid 80 mg per cake sugar syrup honey and condensed milk

Available in cakes of 50 g wrapped in parchment paper or cellophane

ENDOXYCRIN (Endoxycrinum)

Preparation obtained from embryonic tissues Somewhat stimulates oxidizing processes in the body

Prescribed in obesity

Administered orally 2 tablets 2—3 times a day gradually increasing to 5 times a day

Contraindicated in pregnancy and diseases of the kidneys

XIX. BIOGENIC STIMULATORS

ALOE EXTRACT (Extractum Aloës)

Aqueous extract of aloe leaves for subcutaneous injections Preparation for tissue therapy proposed by Academician V P Filatov

Transparent light yellow liquid pH = 5.0—5.6

According to the findings of Academician V P Filatov, extract of aloe leaves that have been kept in the dark at low temperature contains biogenic stimulants which intensify the defensive functions of the body

Use treatment of various ocular diseases (blepharitis, conjunctivitis, keratitis, iritis, cloudiness of hyaloid body, etc), ulcer of the stomach and duodenum bronchial asthma and other diseases

Administered subcutaneously, 1 ml every day (maximal daily dose — 3—4 ml), children up to 5 years old are given injections of 0.2—0.3 ml, children over 5 years old — 0.5 ml The course of treatment consists of 30—35 injections If injections are painful a preliminary injection of 0.5 ml 2% procaine hydrochloride solution is given The course of treatment can be repeated after a break of 2—3 months

In treating patients suffering from bronchial asthma 1—1.5 ml is administered daily for 10—15 days, after which an injection is given each second day The course of treatment consists of 30—35 injections

Available in ampoules of 1 ml

To be stored in a cool, dark place

Rp Extr Aloës 10

D t. d N 15 in amp

S 1 ml subcutaneously

Aloe emulsion (Emulsum Aloës)

Composition juice of aloe leaves previously kept in dark 12 days at a temperature of 6—8° ("biostimulated" by the method of Academician V P Filatov) — 78 parts, castor oil — 11 parts, emulsifier — 11 parts, eucalyptus oil — 0.1 part

Pale cream coloured thick emulsion, characteristic odour

Used for the prevention and cure of skin affections in radiation therapy For prophylactic purposes the emulsion is applied to the skin after each irradiation for therapeutic purposes it is spread in a thin layer on the affected surface 2—3 times a day and covered with a gauze dressing

To be stored in a cool place

FIBS

Preparation obtained by the method of Academician V P Filatov and collaborators "Biological stimulator" prepared from firth mud distillate, contains cinnamic acid and coumarins Sterile preparation

Proposed for the treatment of some ocular diseases blepharitis, conjunctivitis, keratitis cloudiness of the hyaloid body, myopic chorioretinitis etc

Also used for the treatment of arthritis, radiculitis myalgia and other diseases

Administered subcutaneously, 1 ml once a day, 30—35 injections for the course

PELODISTILLATE

Sterile preparation obtained by the method of Academician V P Filatov and collaborators from firth mud Sterile preparation

Indications for use, dosage and length of treatment are the same as for the preparation FIBS

PELOIDIN (Peloidinum)

Extract of medicinal silt. The action is of the "biogenic stimulator" type

Transparent colourless sterile liquid, pH=7.4—7.8

Administered orally in ulcer of the stomach and duodenum gastritis and colitis Prescribed in a dosage of 40—50 ml twice a day (morning and evening) to be taken warm 1—2 hrs before meals or 1—2 hrs after meals To be drunk

in small swallows over a period of several minutes. In colitis also administered in the form of enemas 100 ml twice a day, introduced into the rectum by means of a catheter at a depth of 14–16 cm.

Course of treatment in ulcer of the stomach and duodenum—4–6 weeks in colitis—10–15 days.

Used externally as a lotion and for moistening dressings in the treatment of suppurating wounds.

In acute and subacute adnexitis, periadnexitis, parametritis etc., intramuscular injections of 5–10 ml peloidin warmed to body temperature are given 2–3 times a day for 6–8 days.

It has been reported that oral and intramuscular administration of peloidin is effective in Botkin's disease.

Available in vials and ampoules.

To be stored in a place protected from light.

XX ANTIDOTES AND CHELATE-FORMING COMPOUNDS

UNITHIOL (Unithiolum)

Sodium 2,3-dimercaptopropanesulphonate



BAL



Unithiol

White fine crystalline powder, freely soluble in water.

Available for medical use in the form of a powder or 5% aqueous solution. The solution is a transparent colourless liquid with a faint odour of hydrogen sulphide.

In chemical structure and pharmacological properties, unithiol is similar to dithioglycerol (2,3-dimercaptopropanol) put out in foreign countries under the names BAL, British Anti-Lewisite, Antoxol, Dicapitol.

Unithiol is used for the treatment of acute and chronic poisoning with arsenic (arsenic acid anhydride, sodium arsenate, osarsol, drugs of the novarsenol group etc.), mercury, chromium, bismuth and other metals (except lead) belonging to the so-called thiol poisons, i.e. substances capable of reacting with the sulphydryl (thiol) groups of enzyme proteins and inactivating them. Unithiol like BAL contains two sulphydryl groups. The action of unithiol and BAL chiefly consists in their active sulphydryl groups reacting with thiol poisons in the blood and tissues and forming nontoxic complexes which are excreted in the urine. Binding the poisons restores the function of the body's enzymatic systems that have been affected by them (A. I. Cherkes and N. I. Lugansky).

This mode of action is also the basis for the proposal to use unithiol and BAL for the treatment of hepatolenticular degeneration in the pathogenesis of which a definite role is played by disturbance of copper metabolism in the body and the accumulation of the metal in the nuclei of the striopallidum system (N. V. Konovalov et al.).

Unithiol is less toxic than BAL. Its high solubility in water makes the drug convenient to use and ensures more rapid absorption (BAL is only sparingly soluble in water and therefore is administered intramuscularly in the form of an oil solution).

Unithiol is administered subcutaneously or intramuscularly. Treatment should be begun as soon as possible after poisoning. The single therapeutic dose is 1 ml 5% solution per 10 kg body weight. In cases of poisoning with arsenic compounds, unithiol is given 3–4 times during the first 24 hrs (i.e. every 6–8 hrs), the second day, 2–3 injections are given and after that 1–2 injec

tions per day for 3—7 days. In poisoning with mercuric chloride, the drug is given in the same doses for 6—7 days.

Doses for children from 5 to 10 years old are $\frac{1}{3}$ — $\frac{1}{2}$ those for adults.

When necessary "antidote for metal poisoning" is administered orally along with injections of unithiol, stomach lavage is performed and glucose, oxygen and other medicinal agents prescribed in accordance with the indications.

It has been reported that unithiol and dimercaptopropanol (dicaptol) are effective in treating patients with chronic alcoholism (B. M. Segal). The administration of 1 ml dicaptol intramuscularly or 3—5 ml 5% unithiol solution intramuscularly or subcutaneously 2—3 times a week had a favourable influence on patients' condition and facilitated "antialcohol therapy". Attacks of delirium tremens were aborted by the administration of 1 ml dicaptol or 4—5 ml 5% unithiol solution.

Unithiol is usually tolerated well. In isolated cases nausea, tachycardia, facial pallor and vertigo occur. All these symptoms pass away of themselves.

Available in ampoules containing 5 ml 5% solution and in vials containing 0.5 g dry unithiol. In order to prepare 5% solution the contents of the vial are dissolved in 10 ml isotonic saline or in 10 ml sterile twice distilled water, the contents of the vial are shaken until completely dissolved.

To be stored under ordinary conditions at room temperature.

SODIUM THIOSULPHATE Sodium hyposulfite (Natrium hyposulfurosum)

$\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$

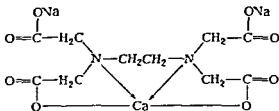
Transparent, colourless crystals, odourless, bitter saline taste, freely soluble in water (1:1), insoluble in alcohol. Dissolves in its water of crystallization at about 50°. The 10% aqueous solution in neutral or weakly alkaline. Solutions are sterilized by holding at 100° for 30 min.

When introduced into the body, sodium thiosulphate has an antitoxic, antiphlogistic and desensitizing effect, administered intravenously, 10—50 ml 10—30% solution in allergic diseases, arthritis, neuralgia and lupus erythematosus. As an antitoxic agent it is used in poisoning with compounds of arsenic, mercury and lead (formation of nontoxic sulfites), hydrocyanic acid and its salts (formation of less toxic thiocyanides) and salts of iodine and bromine.

Used externally for the treatment of scabies by M. P. Demyanovich's method. This is based on the fact that hyposulfite is decomposed in an acid medium with the liberation of sulphur and sulphur dioxide which have an antiparasitic action. 60% hyposulfite solution is rubbed into the skin (successively, for 2—3 min into the skin of the left and right upper extremities, the trunk and the left and right lower extremities—a total of 10—15 min). When the first application has been completed, a halt is made until the skin has dried and crystals of hyposulfite appear. A second application of hyposulfite is then made in the same sequence. When the skin has again dried a 6% solution of hydrochloric acid is rubbed in, pouring it out of the bottle into the palm of the hand, and applying it in the same sequence 3—4 times for 10—15 min, waiting each time for the skin to dry. A bath is permitted in 3 days.

Available in powder form and in ampoules containing 5, 10 and 50 ml 30% solution.

Ethylenediaminetetraacetic acid calcium disodium salt



Synonyms Chelaton EDTA calcium disodium Edatocal, Edathamil calcium disodium Mosatil Versenate calcium disodium

Ethylenediaminetetraacetic acid (EDTA) and its salts belong to the group of complex forming compounds (chelates). These substances form stable water soluble complexes with the ions of heavy metals and the rare earths. The complexes formed in the body when EDTA is administered parenterally are relatively rapidly excreted in the urine.

EDTA calcium disodium salt (EDTA CaNa_2) is a cyclic complex in which Ca can be replaced by the ions of metals with the formation of water soluble compounds of low toxicity which are quickly excreted. Ca can be replaced only by the ions of metals that are more stable than it is such as lead, thorium etc. EDTA CaNa_2 does not react with ions of barium, strontium and the like whose constant of stability is less than that of calcium.

EDTA calcium disodium salt is a white powder, soluble in water.

Used in acute and chronic poisoning with heavy metals and rare earths and their salts (lead, cadmium, cobalt, mercury, uranium, yttrium, cerium etc.).

Administered intravenously by the drip method in isotonic saline or 5% glucose solution. Single dose—2 g (40 ml 5% or 20 ml 10% solution), daily dose—4 g. When administered twice a day the interval between infusions should be at least 3 hrs. Administered daily for 3—4 days followed by a break of 3—4 days. Course of treatment—1 month.

Tablets containing 0.5 g EDTA CaNa_2 can be used for oral administration (in chronic poisoning with lead and other heavy metals). Prescribed in a dose of 1 tablet 4 times a day or $\frac{1}{2}$ tablet 8 times a day. Total drug for the course—20 g. Taken each second or third day. course of treatment—20—30 days. When necessary the course can be repeated but only after the lapse of at least 1 year.

When administered in tablet form the effect is manifested more slowly than when administered intravenously.

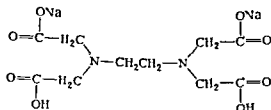
Contraindicated in nephritis, nephrosis and liver diseases with impairment of function. It has been reported that the administration of large amounts of EDTA CaNa_2 (70—60 g) can cause disturbances of the gastrointestinal tract and the kidneys (toxic nephrosis). During treatment there may be a reduction of the hemoglobin content and the concentration of iron and vitamin B₁₂. In acute food poisoning with metals administration of the drug is permissible only after thorough cleansing of the gastrointestinal tract (stomach lavage, siphon, enemas).

It should be borne in mind that the metal complexes formed when EDTA calcium disodium salt is administered are freely soluble and can be absorbed from the gastrointestinal tract. In this way intensifying symptoms of intoxication.

During treatment it is recommended to give iron preparations orally and vitamin B₁₂ parenterally (5—6 injections of 100 µg each second day).

Available in ampoules containing 10 ml 10% solution and in tablets of 0.5 g.

ETHYLENEDIAMINETETRAACETIC ACID DISODIUM SALT



Synonyms Endrate disodium Sequestrene

White fine crystalline powder freely soluble in water

EDTA disodium salt (EDTA Na₂) is a chelate forming compound like EDTA CaNa₂

EDTA Na₂ is capable of forming complexes with various cations including calcium ions. This makes possible its use in diseases accompanied by the superfluous depositing of calcium in the body: pathological ossification of the skeleton, arthritis with deposition of salts, deposition of calcium in the muscles, kidneys and mucosa of the veins, scleroderma, etc.

When using EDTA Na₂ for therapeutic purposes it must be remembered that a therapeutic effect without complications is only achieved when the drug is introduced into the blood stream slowly. Under these conditions the reaction with the calcium in the serum takes place slowly and the concentration of Ca in the serum is not substantially lowered, since the loss is made good by the mobilization of Ca from the tissues, in particular from the bone tissue and superfluous deposits in the body. If the drug is administered rapidly the physiological mechanisms are unable to prevent the lowering of the Ca concentration in the serum and acute tetany may develop.

Because of its ability to bind Ca ions, EDTA Na₂ is likewise used as an anticoagulant when preserving blood.

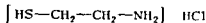
In therapeutic practice EDTA Na₂ is administered intravenously in 5% glucose solution and only by the drip method. 2–4 g dissolved in 500 ml glucose solution is given daily. Drip infusion is performed continuously 3–4 hrs or in divided doses every 6 hours. The course of treatment lasts 3–6 days. If necessary the course is repeated after a 7 day break. During treatment watch must be kept on the Ca concentration in the blood and urine. The diet during treatment should be low in calcium.

When the drug is administered intravenously there may be a burning sensation; this may spread over the entire body and persist for 1–2 hrs after infusion has been completed.

Contraindicated in hemophilia, low coagulability of the blood, hypocalcemia and diseases of the liver and kidneys.

XXI SPECIAL AGENTS FOR THE PREVENTION AND CURE OF RADIATION SICKNESS SYNDROME

MERCAMIN HYDROCHLORIDE (Mercaminum hydrochloricum)
β Mercaptoethylamine hydrochloride



Synonyms: Becaptan, Cysteamine, Lambratene, Mercaptaminum.

White crystalline substance with specific odour of mercaptan, freely soluble in water. Melting point 70–72°.

Mercamin has the ability to weaken the effect of ionizing radiation on the body (in irradiation from without).

Used for the prevention and treatment of the radiation sickness syndrome observed during roentgen and radiotherapy (general malaise, nausea, vomiting, impairment of sense of taste and smell, etc.). It does not prevent the development of leukopenia.

According to present conceptions the action of the drug is based on its anti-oxidizing properties—its ability to bind the free OH groups which are formed in considerable quantities when the body is irradiated. It is also possible that the defensive action is due to the compound's ability to interact with certain enzymes, in particular with SH groups and impart stability to them in respect to radiant energy.

Mercamin hydrochloride is administered intravenously. For prophylactic purposes 1–2 ml 10% solution is injected 10–30 min before the first irradiation.

Additional administrations are made when necessary at intervals of 3, 5 or 7 days. The number of injections for the course is 4, 5 or 7.

For therapeutic purposes when symptoms of radiation sickness have developed, a single or repeated administrations of the drug are given in the same dosage. If the first 2—3 injections give no therapeutic effect, further administration is of no advantage. Intravenous injections of mercamin hydrochloride must be given slowly with the patient lying down. At times there may be some depression of respiration during administration, when necessary in these cases the usual measures are resorted to (use of oxygen, administration of cytolon, caffeine, etc.).

Contraindicated in pronounced impairment of the function of liver and kidneys.

Syringes with glass pistons and stainless steel needles should be used for injections since solutions of mercamin hydrochloride darken on coming into contact with metals and a precipitate may be formed.

Available in ampoules containing 2 ml 10% solution.

To be stored in sealed ampoules in a place protected from light, observing safety precautions (List B).

MERCAMIN SALICYLATE (Mercaminum salicylicum)

White crystalline substance, freely soluble in water and alcohol. Melting point 104—106°.

Similar in mode of action, indications and contraindications to mercamin hydrochloride.

Administered in tablets.

For prophylactic purposes 0.2—0.3 g is given orally 20—30 or 60 min before irradiation daily from the first day till the end of irradiation.

If symptoms of radiation sickness develop the drug is given in the same doses up to 3 times a day — 5—7 times in all for the course. If necessary the prescription is repeated. If no therapeutic effect is manifested during the first 2—3 days further administration is of no advantage.

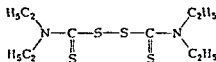
Available in tablets of 0.2 and 0.3 g.

To be stored in tightly closed containers in a cool, dry place, protected from light, observing safety precautions (List B).

XXII. SPECIAL AGENTS FOR TREATING ALCOHOLISM

TETURAM (Teluratum)

Tetraethylthiuram disulfide



Synonyms: Abstynyl, Alcophobin, Antabus, Antaethan, Antaethyl, Aversan, Contrapot, Crotenal, Disetil, Disulfiramum, Espenal, Exhorran, Hoca, Notal, Refusal, Stopethyl, Tetradin.

White crystalline powder, soluble in alcohol, insoluble in water, acids and alkalis. Melting point 70—71°.

Administered orally for the treatment of chronic alcoholism. The action of the drug is based on its ability specifically to influence the metabolism of alcohol. Alcohol is oxidized in the body, passing through the intermediate stage of acetaldehyde and acetic acid. Acetaldehyde is ordinarily quickly oxidized by the enzyme aldehyde dehydrogenase. Teturam blocks aldehyde dehydrogenase, in this way specifically retarding the process of oxidation; this leads to a considerable build up of the concentration of acetaldehyde in the blood when alcohol is ingested. The accumulation of acetaldehyde causes changes in respiration and circulation.

accompanied by unpleasant subjective sensations redness and a sensation of warmth in the face and upper part of the trunk, a feeling of constraint in the chest laboured breathing, a roaring in the head, palpitation a feeling of fright, at times chills, etc. There is a considerable fall in the arterial pressure.

The dosed prescription of teturam is used in conjunction with psychotherapeutic methods in order to develop an aversion to alcohol in patients with chronic alcoholism who are unresponsive to the usual methods of treatment. Treatment with teturam is only carried out in specialized psychoneurological medical institutions.

Only patients under 50 years old are given treatment. Patients are first given a thorough clinical and laboratory examination particular attention being paid to the organs of circulation and respiration.

Absolute contraindications to the use of teturam marked general atherosclerosis, cardiosclerosis, myocarditis, pericarditis, sclerosis of the aorta, diseases of the respiratory organs, pulmonary emphysema, catarrhal bronchitis, exudative pleuritis, sharply manifested forms of pulmonary tuberculosis, diabetes, dysgenitalism, exophthalmic goiter, serious diseases of the central nervous system, kidney diseases, serious diseases of the liver (cirrhosis, hepatitis, atrophy, etc.).

Relative contraindications less serious diseases of the liver, myocardio-dystrophy with impairment of circulation, traumatic affections of the central nervous system.

Before beginning treatment the patient should refrain from ingesting alcohol for 5—10 days after which he is tested for heightened sensitivity to teturam. This is manifested by the appearance of dyspnea, pain in the region of the heart, drowsiness or insomnia, etc., after taking the drug. If tolerance is good, teturam is administered according to the following schedule:

8 A M	6 P M
1st day 0.50 g	0.50 g
2nd " 0.25	0.25
3rd " 0.25 "	0.25 ,
4th " 0.25 "	—
5th " 0.15 "	—

The following days up to a period of 4 weeks 0.15 g is given only in the morning, after which the dose is reduced to 0.1 g and this amount is given for another 2 weeks.

For a month the patient is given 15—30 ml 40% alcohol (vodka) at 11—12 o'clock, that is 3—4 hrs after taking teturam. Alcohol is given each second day, i.e., on the 2nd, 4th, 6th and 8th day of treatment and so on, the amount can be reduced or increased (up to 100%) depending on the strength of the reaction.

Usually the reaction described above develops in 10—15 min after taking alcohol. The ingestion of large amounts of alcohol causes nausea and vomiting. The vascular autonomic reaction ends in sleep lasting 1—8 hrs, after which the patient feels satisfactory.

As treatment proceeds it becomes increasingly unpleasant for the patient to drink alcohol and it finally becomes intolerable for him.

Treatment with teturam is to be carried out only under the observation of a physician. It must be borne in mind that there may be severe reactions during treatment: abrupt fall of arterial pressure, depression of respiration, etc. If there should be cyanosis and dyspnea the patient must be put in a horizontal position and given oxygen or carbogen to inhale. If necessary artificial respiration is started, glucose solution and ascorbic acid administered intravenously and isotonic saline, ephedrine, pentylenetetrazol, camphor or other cardiovascular agents injected subcutaneously. Glucose can also be given intravenously for prophylactic purposes after the end of the reaction.

In order to avoid complications when testing the strength of the teturam alcohol reaction the patient should not be given more than 15—30 ml 40% alcohol. After taking alcohol the patient must remain in a sitting or recumbent position and should be under the observation of medical personnel for at least 6—8 hrs since remote side effects sometimes occur.

Findings have recently been published concerning psychoses observed in isolated cases after the use of teturam (I. V. Strechuk et al). In such cases a therapeutic effect was obtained with sleep, the administration of chlorpromazine and general disinfecting therapy (intravenous infusion of glucose and ascorbic acid, inhalation of oxygen, administration of vitamins B₁ and B₂, etc).

Available in powder form and in tablets of 0.1, 0.15 and 0.25 g.

To be stored in a place protected from light, observing safety precautions (List B).

Chapter IX

ANTIMICROBIC AND ANTIPARASITIC AGENTS

1 CHEMOTHERAPEUTIC AGENTS

A Antibiotics

ALBOMYCIN (Albomycinum)

Antibiotic produced by growth of the microorganism Streptomyces subtrypicus

Yellow or brown powder soluble in water decomposes on heating

Inhibits the growth of gram positive and some gram negative bacteria staphylococci pneumococci Friedlander's pneumobacteria dysentery and colibacilli etc. It is less active against streptococci

Effective against penicillin resistant strains of staphylococci pneumococci and some other microbes

Use treatment of pneumonia of diverse etiology in children and adults secondary pneumonia after influenza measles and whooping cough complications after dysentery colenteritis toxic dyspepsia and other gastrointestinal diseases (pneumonia otitis pyelitis etc) various septic conditions (abscesses sepsis etc) infectious skin affections (pyoderma) Can be used for the treatment of diseases caused by penicillin resistant forms of staphylococcus and pneumococcus It has also been reported that albomycin is effective in tick borne relapsing fever

Available in ampoules of 1 000 000 and 5 000 000 units

The contents of the ampoules are dissolved in 2—5 ml sterile twice-distilled water isotonic saline or 0.5—1% procaine hydrochloride Solutions must be injected immediately they must not be kept in opened ampoules

The antibiotic is administered subcutaneously or intramuscularly usually at the rate of 100 000—200 000 units per kg body weight per day The daily dose is given in two injections at intervals of 12 hrs Course of treatment 7—20 days

In surgical practice a solution of albomycin is sometimes instilled into the abdominal cavity (through the drainage tube) in severe peritonitis at a rate of 10 000 000—20 000 000 units in 24 hrs in addition 2 subcutaneous injections of 5 000 000 units are given daily

Ointments containing albomycin can be used in skin diseases

Other antibiotics and sulfanilamide drugs can be prescribed simultaneously with albomycin

Albomycin is usually tolerated well, it is only in isolated cases that allergic reactions may occur and these pass away when the antibiotic is withdrawn or antihistamines administered

To be stored in sealed ampoules at a temperature not higher than 10°C

Rp Albomycini 1 000 000 units

D t d N 10 in amp

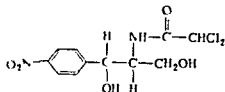
S Dissolve contents of ampoule in 2 ml twice distilled water

Fresh solution to be injected subcutaneously 1.5 ml every 12 hrs (for a child weighing 7.5 kg)

LEVOMYCETIN (Levomycesinum)

Synthetic substance identical with the natural antibiotic, chloromycetin (chloramphenicol), which is produced by the growth of the microorganism *Streptomyces venezuelae*

Chemically levomycetin is D (—) threo 1 (p nitrophenyl) 2 dichloroacetamido 1,3 propanediol



Synonyms Allicetin Berliceline Biophenicol Chemicein Chloramphenicol, Chlorocyclina Chloromycetin Chlorinitrin Detreomycin Globenicol Halomycetin Leukomycin Paraxin, Synthomycetin, Typhomycin

White crystalline powder bitter taste sparingly soluble in water freely soluble in alcohol propylene glycol and ethyl acetate Melting point 148—151°

Levomycesin is an antibiotic with a wide antimicrobial spectrum it is effective against many gram positive and gram negative bacteria rickettsiae and spirochetes as well as some large viruses it acts on strains of bacteria insensitive to penicillin streptomycin and sulfanilamides Levomycesin is easily absorbed from the gastrointestinal tract After oral administration the maximal concentration in the blood is achieved in 2—4 hrs An active blood concentration is sustained for 6—8 hrs after a single therapeutic dose after which the concentration falls considerably Administrations must be given every 6—8 hrs in order to maintain a constant blood level Excreted for the most part in the urine in the form of transformation products partially excreted unchanged

Use typhoid and paratyphoid fever dysentery brucellosis whooping cough pneumonia gonorrhea purulent infections tularemia and some other bacterial infections typhus and other rickettsioses, trachoma psittacosis and other diseases caused by large viruses

Levomycesin is administered orally in powders or tablets 20—30 min before meals Because of the bitter taste it is often given to children in jam honey jelly or rice water In pediatric practice eulevomycesin is more convenient since it has no bitter taste

In cases of persistent vomiting the drug can be administered in the form of suppositories but doses must be increased 50%

For the treatment of trachoma an emulsion of levomycesin or synthomycin is used

Doses of levomycesin and length of treatment depend on the character and course of the disease the patient's age and the extent to which the drug is tolerated

For oral administration the single dose for adults ranges from 0.25—0.75 g usually 0.5 g is given During the first few days of the disease the drug is administered up to 6 times a day when the temperature subsides and the general

condition improves the number of doses is reduced to 3—4. Treatment is usually for 4—10 days, but in diseases marked by relapses it is for 2—3 weeks. Treatment should be continued for several days after the normalization of the temperature and the disappearance of all symptoms of the disease.

In the treatment of acute dysentery, adults are usually prescribed 0.5 g levomycetin every 6 hrs (2 g per 24 hrs) for 5—7 days, if recovery is not complete, the course of treatment is repeated in 3—5 days. Levomycetin can be administered in combination with sulfanilamide drugs — phthalazol or sulgin — according to the following schedule:

1st day levomycetin, 0.75 g 4 times, phthalazol (or sulgin) 1 g
5 times

2nd day levomycetin, 0.5 g 4 times, " " " " 1 g
5 times

3rd 5th day levomycetin, 0.25 g 4 times " " " " 1 g
4 times

6th 7th day " 0.25 g 4 times " " " " 1 g
4 times

If necessary the course of treatment can be repeated after a 3—5-day break.

In chronic dysentery levomycetin is administered according to one of the schedules indicated over a period of 7—14 days, treatment with levomycetin can be combined to advantage with vaccinothérapie, with other antibiotics (streptomycin) and with sulfanilamides. The course of treatment is repeated if warranted by the indications.

In typhoid fever, levomycetin is administered in a dose of 0.75 g every 6 hrs (3 g per 24 hrs) until the temperature subsides and for 3—4 days afterwards, then the dose is reduced to 0.5 g 4 times a day (2 g per 24 hrs), during the next 2 days the dose is 0.25 g. Treatment is carried out continuously until the temperature is normal over a period of 8—10 days.

In cases of food toxoinfections, the drug is prescribed in a dose of 0.5 g every 6 hrs until the temperature falls and for 2—3 days afterwards, stomach lavage is performed before beginning treatment.

In brucellosis, levomycetin is given in a dose of 0.75 g every 6 hrs for 10—15 days, after a break of 10—15 days the course of treatment is repeated.

In typhus, the dose is 0.5—0.75 g every 6 hrs until the temperature falls and for 2—3 days afterwards.

Levomycetin is extremely effective in the treatment of gonorrhea. In acute anterior and total urethritis in males and females, 5 g is prescribed in a 2 day course (doses of 0.5 g, 3 g the 1st day and 2 g the 2nd). In gonorrhea with complications 6—7 g is given for the course (doses of 0.5 g timed so that the night break in treatment does not exceed 7—8 hrs).

Maximal doses for adults: single — 1 g, daily — 4 g.
Children are given levomycetin in smaller doses: up to 3 years old — doses of 0.01—0.015 g (10—15 mg) per kg body weight, 3—4 times a day, from 3—8 years — doses of 0.15—0.2 g, over 8 years — doses of 0.2—0.3 g.

Children are often prescribed levomycetin in dysentery and other intestinal infections, pneumonia, angina, otitis, whooping cough, etc.

In severe cases of dysentery treatment is begun with a "shock" dose, for children weighing up to 15 kg this is equal to the daily dose (given in two portions, the second 1 hr after the first). Administration of the drug is then continued in the doses indicated. For children weighing over 15 kg the shock dose is 0.5—1 g (also given in two portions).

In protracted and chronic dysentery streptomycin is given simultaneously (up to 20,000 units per kg body weight, but not more than 200,000 units in 24 hrs) and vaccinothérapie is also resorted to.

Maximal doses of levomycetin for children up to 5 years old, single — 0.02 g per kg body weight, daily — 0.12 g per kg body weight,

5-6 years single — 0.2 g, daily — 1.2 g, 7-9 years, single — 0.25 g, daily — 1.5 g, 10-14 years, single — 0.3-0.4 g, daily — 1.8-2 g

As with other antibiotics, treatment with levomycetin should be carried out only on the prescription of a physician and under his observation. It must be remembered that giving the drug in insufficient doses, or stopping treatment too soon may lead to the appearance of resistant strains of the causative organism insensitive in future to the action of the antibiotic. Moreover, when using levomycetin allergic symptoms and other side effects may occur: hyperemia and irritation of the mucous membranes of the mouth, pharynx, genitalia and anus, dermatitis, skin eruptions, dyspeptic disorders, changes in the blood. If side effects are sharply manifested, administration of the drug must be discontinued.

The lengthy administration of levomycetin may lead to the development of fungous affections of the skin and mucous membranes, fungous foci in the lungs and fungous septicemia (candidamycosis), just as in the case of other antibiotics and especially combinations of antibiotics (see Biomycin).

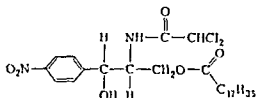
Levomycetin is contraindicated in psoriasis, eczema, and fungous and other skin diseases, as well as in cases of heightened sensitivity to the drug.

Available in powder form and in tablets of 0.1, 0.25 and 0.5 g.

To be kept in stoppered bottles in a place protected from light, observing safety precautions (List B).

EULEVOMYCETIN (Eulaevomycetinum)

Stearic ester of levomycetin (levomycetin without the bitter taste)



Amorphous yellowish cream coloured powder, insoluble in water, sparingly soluble in alcohol. Melting point 87-89°. Contains 55% levomycetin. Does not have bitter taste of levomycetin.

Eulevomycetin is saponified in the gastrointestinal tract with liberation of levomycetin, its active principle. The concentration of levomycetin in the blood is built up more slowly when eulevomycetin is administered than is the case with levomycetin and remains at a lower level if equal doses are used. Eulevomycetin is not absorbed completely from the gastrointestinal tract, and consequently a bacteriostatic concentration is maintained in the intestine for a longer time.

Indications for the use of eulevomycetin are the same as for levomycetin: dysentery, typhoid fever, whooping cough, angina, otitis, pneumonia and other infectious diseases. Eulevomycetin is mostly used in pediatric practice when the administration of levomycetin is difficult because of the bitter taste.

Administered orally. Doses for children and adults are fixed on the basis of the levomycetin content (1 g eulevomycetin contains 0.55 g levomycetin). Doses are arrived at practically by doubling doses of levomycetin. Frequency of administration and length of treatment are the same as for levomycetin. It is advisable to give the drug to children up to 2-3 years old in their porridge or milk.

The side effects are the same as with levomycetin, with the exception of those which depend on the bitter taste of the latter.

Available in powder form in tablets of 0.25 g, granules (50% eulevomycetin and 50% sugar) and 5% sweet syrup (1 teaspoonful contains 0.25 g eulevomycetin).

To be stored in well closed glass containers in a dry place protected from light observing safety precautions

SYNTHOMYCIN (Synthomycinum)

Identical with levomycetin in chemical structure. The latter is the levorotatory isomer of threo 1 (p nitrophenyl) 2 dichloroacetamido 1,3 propanediol while synthomycin is the racemic form.

The active principle of synthomycin is levomycetin. The dextrorotatory isomer (dextromycetin) has no antibiotic activity.

White crystalline powder bitter taste practically insoluble in water sparingly soluble in alcohol. Melting point 149—153.

Similar to levomycetin in antimicrobial spectrum and in chemotherapeutic activity and is used in the same indications but larger doses are given (0.5, 0.75 or 1 g for adults). The frequency of administration and the length of treatment are the same as when levomycetin is used.

Children up to 3 years old are prescribed a dose of 0.02 g per kg body weight 3—4 times a day (every 6 hrs or every 4 hrs in the daytime with an 8 hour break at night). Children over 3 years old are given doses of 0.3—0.5 g depending on the age. The drug is given 20—30 min before meals.

In severe cases of dysentery treatment with synthomycin is begun with a shock dose for children weighing up to 15 kg this is equal to the daily dose while for children weighing over 15 kg it is 0.5—1 g. The shock dose is given in 2 portions the second 1 hr after the first.

In cases of persistent vomiting synthomycin can be administered in the form of suppositories but the dose should be increased 50%.

Maximal doses of synthomycin for adults single—15 g daily—6 g.

Maximal doses for children up to 5 years old single—0.02 g per kg body weight daily—0.12 g per kg body weight 5—6 years single—0.2 g daily—1.2 g 7—9 years single—0.3 g daily—1.8 g 10—14 years single—0.4—0.5 g daily—2.4—3 g.

The same complications may occur when using synthomycin as when using levomycetin in addition complications have been noted involving the nervous system, such as excitement a feeling of fright and other disturbances these symptoms pass away in 2—3 days after withdrawal of the drug.

Contraindications are the same as for levomycetin.

Available in powder form and in tablets of 0.1, 0.25 and 0.5 g.

To be kept in a place protected from light observing safety precautions (List B).

Synthomycin emulsion (Emulsio Synthomycin) Used for the treatment of suppurating wounds purulent inflammatory diseases of the skin and mucous membranes trachoma and syphilis.

Composition 1% 5% or 10% synthomycin castor oil emulsifier distilled water preservative. For treating wounds an emulsion is also available containing procaine hydrochloride in addition.

Instead of synthomycin emulsion an emulsion containing levomycetin can likewise be used.

Synthomycin emulsion is of the consistency of thick cream.

The emulsion is applied locally to the wound or affected area in purulent affections of the skin furunculosis carbuncles suppurating wounds keratoconjunctivitis unhealing ulcers II and III degree burns fissures in the nipples of nursing mothers etc. The emulsion is covered with an ordinary bandage compress or parchment paper may be used.

When using 1% emulsion the dressing is changed in 2—3 days when using 10% emulsion in 4—5 days. Treatment is continued until the wound heals. Surgical intervention is performed in accordance with the initial indications after which treatment with synthomycin emulsion is begun.

In treating trachoma a 10% (or 1%) emulsion of synthomycin or levomycetin is used.

In simple forms of I, II and III stage trachoma without ulceration of the cornea, treatment is begun with thorough expression of the conjunctiva of the lids, the fornices, the lacrimal sac and the semilunar fold in aseptic conditions with ordinary dicain anesthesia (1—2 drops of 1% solution in the conjunctival sac), the emulsion is then rubbed into the conjunctiva of the lids and the fornices with a glass rod after first drying with a wisp of cotton and removing traces of blood, etc. The emulsion is applied under the lids before retiring. Subsequently the emulsion is applied to the conjunctival sac twice a day.

About 0.3—0.5 g emulsion is used per day, making 15—25 g for a 2 month course of treatment.

In trachoma with ulcers of the cornea as a complication the ulcers should first be treated by applying the emulsion to the conjunctival sac 3—4 times a day, 7—10 days are usually necessary for complete epithelization, this is followed by expression of the conjunctiva and the course of treatment with synthomycin emulsion.

When there is acute conjunctivitis arising from secondary microbial infection, the emulsion should be applied under the lids 3—4 times a day for 3—5 days (until symptoms of acute conjunctivitis disappear), after which expression is performed, followed by application of the emulsion and massage with a glass spatula twice a day. In most cases the length of treatment can be limited to 60 days.

After completing the course of treatment, patients should be examined by an ophthalmologist at least once in 2 months.

Patients with trachoma who are not completely cured after two months should continue treatment with the emulsion for another two months; if treatment is not completely successful after 4 months, a break of 1—2 months should be made to rest the patient, after which the course of treatment should be repeated on an inpatient basis.

Available in tightly closed jars of 10, 20, 60 and 100 g

EUSYNTHOMYCIN (Eusynthomycinum)

Stearic ester of synthomycin ("synthomycin without the bitter taste")

Greyish green powder, insoluble in water, soluble in organic solvents, does not have the bitter taste of synthomycin. Melting point 84—87°. Contains about 55% bound synthomycin.

In chemical structure and action, eusynthomycin is related to synthomycin in the same way as eulevomycetin is related to levomycetin.

The fact that eusynthomycin is not bitter makes it more convenient to use than synthomycin, particularly in pediatric practice.

Eusynthomycin can be used in all cases where synthomycin is indicated, especially in dysentery, typhoid fever, whooping cough, pneumonia, and staphylococcal and streptococcal infections.

Eusynthomycin is given in larger doses than synthomycin, since only part of its molecule is synthomycin.

The single dose for adults is 1—2 g. Children weighing up to 10 kg are given doses of 0.03 g per kg body weight, children weighing over 10 kg are given doses of 0.35—0.5 g. The frequency of administration and the length of treatment are the same as when synthomycin is used. For infants up to 2 years old it is advisable to administer the drug in their porridge or milk.

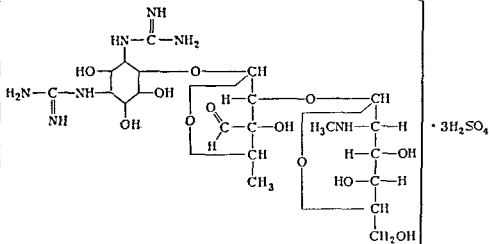
The same complications are possible when using eusynthomycin as when using synthomycin, with the exception of those depending on the bitter taste of the latter. If complications occur the dose is reduced or the drug withdrawn completely.

Available in powder form and in tablets, granules and syrup.

To be stored in well stoppered glass containers in a place protected from light observing safety precautions (List B).

STREPTOMYCIN SULPHATE (Streptomycinum sulfuricum, Streptomycin sulfas)

Streptomycin is an antibiotic substance produced by the filamentous fungus, *Actinomyces globisporus streptomycini*, or other related organisms. It has the following structure



Streptomycin sulphate

Synonyms Strepolin, Strepsulfat, Streptaquine, Strycin, Strysolin

In medical practice streptomycin sulphate and the streptomycin-calcium chloride complex are used

Streptomycin sulphate white or almost white powder or porous mass, odourless, slightly bitter taste, hygroscopic freely soluble in water, practically insoluble in alcohol chloroform and ether. Stable in weakly acid medium but easily destroyed in solutions of strong acids and alkalis, and when heated

Doses of streptomycin are calculated on the basis of weight or units of activity 1 unit = 1 microgram ($1\mu\text{g} = 0.000001\text{ g}$) chemically pure streptomycin base.¹

Streptomycin inhibits the vital activities and reproduction of sensitive gram positive and gram negative bacteria, as well as acid resistant microbes, it is also effective against penicillin resistant forms

Use tuberculosis of the lungs, lymph nodes, mouth, larynx, trachea, bronchi, intestine, genitourinary organs, serous membranes, bones, joints, eyes and skin (lupus), tuberculous meningitis and meningitis caused by other streptomycin sensitive microbes (bacteria of the coli and paratyphoid groups, *Pseudomonas pyocyanea*, etc.), peritonitis, pleuritis diseases of the urinary tract caused by streptomycin sensitive microbes, endocarditis caused by penicillin resistant microbes, gonorrhea, whooping cough, tularemia, brucellosis, plague

Streptomycin is more effective in early and acute forms of the tuberculous process, as well as in initial forms of a primary complex fresh infiltrative broncho adenitis, infiltrative pneumonic pulmonary tuberculosis and especially acute miliary and subacute hematogenic disseminated pulmonary tuberculosis. Treatment is less effective in focal and exacerbated chronic disseminated proce

¹ Salts of streptomycin (or dihydrostreptomycin) contain different amounts of streptomycin (or dihydrostreptomycin) base depending on the molecular weight and number of molecules of the anion as well as the purity of the preparation. In practice when prescribing preparations 1 microgram of each preparation is often considered equal to 1 unit of activity. Theoretically 1 mg streptomycin sulphate contains 800 units while 1 mg of the calcium chloride contains 780 units.

ses Streptomycin is contraindicated in focal pulmonary tuberculosis in the phase of consolidation in the absence of an exacerbation of the process in patients with cirrhotic pulmonary tuberculosis in quiescent forms of tuberculosis of the bones and joints in diseases caused by anaerobic microbes rickettsiae plasmodia and viruses

Streptomycin sulphate is administered by intramuscular injection and by instillation into cavities. The sulphate is not used for injections into the spinal canal but only the calcium chloride complex.

Dosage of streptomycin for intramuscular administration adults—from 500 000 (0.5 g) to 1 000 000 units (1 g) in 24 hrs children up to 3 years old—200 000—250 000 units daily from 4 to 7 years—250 000—300 000 units from 8 to 12 years and older—300 000—500 000 units

Maximal doses of streptomycin (sulphate and calcium chloride complex) administered intramuscularly for adults single—1 g (1 000 000 units) daily—2 g (2 000 000 units)

Maximal doses for children up to 5 years old single—0.1—0.125 g (100 000—125 000 units) daily—0.2—0.25 g (200 000—250 000 units) 5—6 years single—0.125—0.15 g (125 000—150 000 units) daily—0.25—0.3 g (250 000—300 000 units) 7—9 years single—0.15—0.175 g (150 000—175 000 units) daily—0.3—0.35 g (300 000—350 000 units) 10—14 years single—0.2—0.25 g (200 000—250 000 units), daily—0.4—0.5 g (400 000—500 000 units)

The daily dose of streptomycin solution is given in 1 or 2 injections into the buttocks or the thigh muscle.

Streptomycin can be prescribed simultaneously with other medicines. When treating tuberculosis it is often administered in combination with phthivazid PAS and other chemotherapeutic drugs.

The length of treatment with streptomycin is fixed individually for each patient depending on the character of the disease, the effectiveness of the drug and the tolerance shown for it. In acute miliary tuberculosis treatment averages 1—5 months in infiltrative forms—3—4 months in a focal process—2—3 months. Longer courses of treatment are also given—up to 6, 12 or 18 months.

In the treatment of brucellosis 500 000 units are administered twice a day for 20 days in tularemia—the same dose for 4—7 days. In acute gonorrhea 500 000 units are given twice in 24 hrs the second injection 8—12 hrs after the first the same dose (1 000 000 units) can be given for 2 days 500 000 units per day (in one or two injections) if there should be complications the dose for the course is increased to 2 500 000—5 000 000 units (2.5—5 g).

In the chronic form of dysentery and in bacilli carriers streptomycin is administered in conjunction with levomycetin and vaccine. In treating children with a chronic form of dysentery streptomycin is given orally with ecmolin every day for a period of 10 days after a 10 day break a second cycle of treatment of the same length and with the same dosage is given. For children weighing up to 15 kg the dose of streptomycin is calculated at the rate of 15 000 units per kg body weight daily. For children weighing more than 15 kg the daily dose is 200 000—300 000 units. Children over 15 years old and adults are prescribed 300 000—500 000 units daily. The streptomycin is dissolved in 20 ml 0.5% ecmolin solution. The daily dose is given in 4 portions during the day (with a break at night). In exacerbations of chronic dysentery a favourable effect is frequently observed when streptomycin is injected intramuscularly in a dose of 125 000 units 4 times a day for 5—6 days.

Streptomycin is an effective remedy for tuberculosis of the skin. It is injected intramuscularly in a daily dose of 500 000—1 000 000 units. The dose for the course of treatment is 50 000 000—70 000 000 units. To accelerate cicatrization streptomycin can be used topically along with intramuscular injections 200 000—400 000 units are applied to the focus of affection once in 4—6 days. For intramuscular administration streptomycin is dissolved in 2—3 ml sterile

isotonic saline, twice distilled water or 0.25—0.5% procaine hydrochloride solution. Freshly prepared solutions must be used.

In pulmonary tuberculosis and inflammatory diseases of the lungs, streptomycin can be used in the form of an aerosol (0.1—0.2 g streptomycin in 1—2 ml isotonic saline per inhalation). Inhalations are carried out daily or each second day, on the average, 15—20 inhalations are prescribed for the course. Streptomycin can likewise be administered intratracheally, 0.25—0.5 g in 2 ml isotonic saline (after anesthesia of the mucous membranes of the respiratory passages).

In peritonitis a solution of streptomycin and penicillin is instilled into the abdominal cavity, in suppurative and exudative pleuritis the solution is instilled into the pleural cavity. The dose is 250,000—500,000 units in 5—10 ml sterile distilled water.

During treatment with streptomycin there may be tenderness at the site of injections. Relatively often drug fever, dermatitis and other allergic symptoms occur, as well as vertigo, headache, palpitation, albuminuria and hematuria, diarrhea may result from the inhibition of the microflora of the intestine. The most serious complications are vestibular disturbances and impairment of hearing, the lengthy administration of large doses may lead to deafness.

Treatment with streptomycin should be carried out under the careful observation of a physician, prior to treatment and regularly during treatment the function of the VIII pair of cerebral nerves, and the vestibular and acoustic apparatus must be examined and watch kept on the function of the kidneys and the blood formula.

In cases of mild side effects, the dose of the antibiotic should be reduced, it is advisable to administer dimedrol, 0.03—0.05 g 2—3 times a day, along with calcium chloride, as well as vitamin B₁. If side effects are pronounced, treatment must be stopped.

In persons coming into contact with streptomycin for lengthy periods (pharmaceuticalists, nurses, and persons engaged in the manufacture of the drug) contact dermatitis may develop. In order to avoid this, the necessary precautionary measures must be taken (gloves, respirator and protective goggles must be worn, etc.).

Available in vials hermetically closed with rubber stoppers supplied with metal caps. Vials contain 0.25, 0.5 or 1 g streptomycin.

To be stored in the original containers in a cool, dry, dark place (at a temperature not higher than 20°).

STREPTOMYCIN-CALCIUM CHLORIDE COMPLEX (Streptomycini et Calcii chloridum; Streptomycinum calcium chloratum)

Streptomycin calcium chloride complex is a special form of streptomycin which is mostly used for the treatment of tuberculous meningitis and meningitis caused by other streptomycin sensitive microbes (bacteria of the coli and paratyphoid groups, *Pseudomonas pyocyanea*, etc.). White crystalline powder or porous mass, freely soluble in water.

Chiefly used for subarachnoidal administration. The preparation can also be administered intramuscularly like streptomycin sulphate.

Indications and contraindications for the intramuscular administration of the calcium chloride complex are the same as for the sulphate.

In meningitis, streptomycin calcium chloride complex is administered endolumbarly in the following single doses: children up to 1 year old — 10,000—15,000 units, from 1 to 3 years — 15,000—25,000 units, from 4 to 7 years — 25,000—50,000 units, from 8 to 12 years — 50,000—75,000 units, older children and adults — 75,000—100,000 units.

Suboccipital administrations are given in the following single doses: children up to 1 year old — 10,000—20,000 units, from 1 to 2 years — 20,000—30,000 units, from 2 to 6 years — 30,000—40,000 units, from 6 to 8 years — 40,000—50,000 units, from 8 to 12 years — 50,000—75,000 units, older children and adults — up to 100,000 units.

The preparation is administered once a day. In subarachnoidal administration three cycles of injections are first given 1 injection per day for 5—6 days with a break of 1 day between cycles — a total of 15—20 injections. Injections are then given each second or third day. The total number of injections comes to 50—60. While receiving spinal injections of streptomycin calcium chloride complex patients with tuberculous meningitis should simultaneously be given intramuscular injections of streptomycin (sulphate of calcium chloride complex).

Solutions for subarachnoidal administration are prepared *ex tempore* with sterile freshly prepared twice distilled water or isotonic saline. A solution containing 10 000 units per *ml* is first prepared by dissolving 0.1 g powder in 10 *ml* twice distilled water or isotonic saline; this is drawn into the syringe and another 2—5 *ml* distilled water or isotonic saline added.

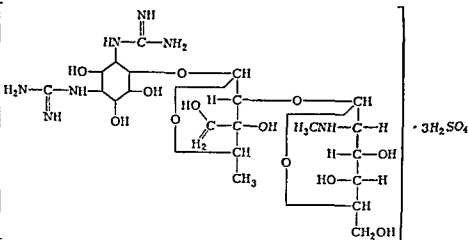
When using streptomycin calcium chloride complex the same allergic and neurotoxic complications may occur as when the sulphate is used; moreover complications arising from the introduction of the drug into the spinal canal are likewise possible (changes in the meninges and the spinal fluid etc.). The lumbar punctures themselves are not infrequently badly tolerated by patients. Lately because of the appearance of new effective antituberculosis drugs (phthivazid and others), there has been a tendency to limit the subarachnoidal administration of streptomycin or to discontinue it completely. It is recommended that streptomycin should be injected into the spinal canal only in neglected cases when the patient's condition hinders the administration of phthivazid, PAS and other antituberculosis drugs.

Available in vials hermetically closed with rubber stoppers supplied with metal caps containing 100 000, 200 000 or 500 000 units of streptomycin.

To be stored in the original containers in a cool dark dry place (at a temperature not higher than 20°).

DIHYDROSTREPTOMYCIN (*Dihydrostreptomycinum*)

Produced by the reduction of streptomycin, the aldehyde group being converted into the methanol group.



Dihydrostreptomycin sulphate

Dihydrostreptomycin sulphate: white powder or dry porous mass (at times with slight yellow tint); freely soluble in water. Decomposed by acids; more

stable in solutions of alkalis than streptomycin. Somewhat less toxic than streptomycin and tolerated better by some patients.

Indications and contraindications for the use of dihydrostreptomycin are the same as for streptomycin. Microorganisms resistant to streptomycin are likewise resistant to dihydrostreptomycin.

Administered intramuscularly. Doses are fixed individually, depending on the character and form of the disease, the patient's age, the efficacy of treatment and the extent to which the drug is tolerated. Doses for adults range from 0.5 to 1 g per day. Daily doses for children up to 3 years old — 0.2–0.25 g, from 4 to 7 years — 0.25–0.3 g, from 8 to 12 years — 0.3–0.5 g. Solutions are prepared immediately before use. The necessary amount of the drug is dissolved in 2–3 ml sterile isotonic saline, twice distilled water or 0.25–0.5 % procaine hydrochloride solution.

When warranted by the indications, dihydrostreptomycin can be used in combination with phthivazid, PAS, penicillin or other antibacterial drugs.

Dihydrostreptomycin is usually tolerated better than streptomycin and vestibular disturbances and impairment of hearing are encountered less frequently. Allergic reactions may occur: dermatitis, fever, slight eosinophilia, dyspeptic symptoms. Caution must be observed when administering the drug in cases of kidney diseases (acute nephritis) because of the consequent delay in excretion.

Treatment should be carried out under the careful observation of a physician prior to and during treatment; watch must be kept on the condition of the VIII pair of cerebral nerves, the vestibular and acoustic apparatus, on the function of the kidneys and on the blood formula.

Available in hermetically closed vials containing 0.25, 0.5 and 1 g.

To be kept in a cool place protected from light (at a temperature not higher than 20°).

DIHYDROSTREPTOMYCIN PAS

Dihydrostreptomycin para-aminosalicylate contains dihydrostreptomycin and para-aminosalicylic acid in the molar proportion of 1 : 3.

Yellow powder or dry porous mass, freely soluble in water, decomposes under the action of acids, alkalis and light.

Chiefly used in the treatment of tuberculosis. Can likewise be used in non-specific postoperative pneumonia and in suppurative processes caused by streptomycin-sensitive microbes, particularly in persons who have had tuberculosis. When necessary, can be prescribed simultaneously with phthivazid, penicillin or other antibacterial drugs.

Administered by intramuscular injection or by instillation into body cavities. The daily dose for adults, intramuscularly, is 0.5–1 g. Children are given 0.1–0.5 g daily, depending on the age. The length of treatment depends on the character of the disease and the efficacy of treatment. The dose for instillation into fistulas and cavities is 0.25–0.5 g; the drug is dissolved in 2–3 ml 0.25–0.5 % procaine hydrochloride or distilled water. Fresh solutions are used.

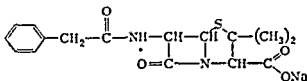
During treatment with the drug, the possibility of disturbances of the function of the vestibular apparatus and changes in hearing must be borne in mind. Allergic reactions may occur. Contraindications are the same as for streptomycin and dihydrostreptomycin.

Available in vials containing 0.25, 0.5 and 1 g. To be stored at a temperature not higher than 20°.

PENICILLIN (Penicillium) BENZYL PENICILLIN

Penicillin is an antibiotic produced by the growth of various species of the mold *Penicillium* (*P. notatum*, *P. chrysogenum*, etc.). Various forms of penicillin are produced during the growth of these molds, differing from one another in chemical structure and antibacterial activity. The most potent is benzylpenicillin.

Penicillin is an acid. In medical practice the sodium and other salts of benzylpenicillanic acid are used. The sodium salt has the following structure:



Other forms of penicillin differ from benzylpenicillin in having different radicals in place of the benzyl group ($-\text{CH}_2-\text{C}_6\text{H}_5$).

At present the following preparations of penicillin are being used: a) crystalline benzylpenicillin sodium (Benzylpenicillinum natrium crystallisatum), b) crystalline benzylpenicillin potassium (Benzylpenicillinum kalium crystallisatum), c) benzylpenicillin procaine, d) benzylpenicillin N, N' — dibenzylethylenediamine (bicillin), e) phenoxymethylpenicillin, f) econovocillin.

The crystalline sodium and potassium salts of benzylpenicillin are white, fine crystalline powders, odourless, bitter taste, slightly hygroscopic; very freely soluble in water, soluble in alcohol. Easily destroyed by boiling in aqueous solution, and by the action of acids, alkalis, oxidizing agents and the specific enzyme, penicillinase. Solutions are slowly decomposed at room temperature but are stable to sunlight.

The potency of penicillin is expressed in units of activity. One unit corresponds to the activity of 0.5988 μg chemically pure crystalline benzylpenicillin sodium. Activity is determined by the biological method and is based on the antibacterial effectiveness against a certain strain of *Staphylococcus aureus*. Theoretically 1 mg of benzylpenicillin sodium can contain 1667 units, and 1 mg of the potassium salt, 1600 units. Practically, both preparations are put out with an activity not less than 1550 units. Penicillin has a broad spectrum of antibacterial action. It is effective against streptococci, pneumococci, meningococci, gonococci, spirochetes and other causative organisms. It is less effective against staphylococci. It is not effective against viruses (smallpox, poliomyelitis, influenza virus, etc.), coli bacilli or the causative organisms of tuberculosis, brucellosis and amebiasis.

Penicillin is quickly absorbed when administered intramuscularly, the maximal concentration in the blood is reached in 30–60 min. When administered subcutaneously, the speed of absorption is less constant, but usually the maximal concentration in the blood is achieved in 60 min. In 3–4 hrs after a single intramuscular or subcutaneous administration only traces of the antibiotic are to be found in the blood. In order to maintain the concentration at a sufficiently high level for a therapeutic effect, injections must be made every 3–4 hrs.

When injected intravenously the concentration in the blood falls rapidly. When administered by mouth penicillin is absorbed badly and is destroyed by the gastric juice and by the enzyme, penicillinase, which is produced by the microflora of the intestine. Penicillin is excreted for the most part by the kidneys.

Use: croupous and focal pneumonia, subacute septic endocarditis, wound infections, purulent infections of the skin, soft tissues and mucous membranes, suppurative pleuritis, peritonitis, cystitis, septicemia and pyemia, acute and chronic osteomyelitis, various forms of angina, diphtheria, erysipelas, inflammation of the middle ear, inflammatory diseases of the eye, epidemic cerebrospinal meningitis, scarlatina, gonorrhea, blenorhea, syphilis, anthrax, other infectious diseases caused by penicillin-sensitive microorganisms. In other cases, including influenza without concurrent bacterial infection, the use of penicillin is not rational and is not completely safe because of possible side effects.

Solutions of the crystalline sodium and potassium salts of benzylpenicillin are injected intramuscularly or subcutaneously, when necessary they are injected

intravenously or instilled into cavities (abdominal pleural etc.) In diseases of the lungs they are also used in the form of aerosols and in ocular diseases in the form of eye drops and subconjunctivally

Of all the preparations of benzylpenicillin it is only the sodium salt that is used for endolumbar injections. Other penicillin preparations are not used for this purpose.

Penicillin solutions are prepared with sterile isotonic saline or distilled water. Often in order to prolong the action penicillin solutions are prepared with 0.25, 0.5 or 1% procaine hydrochloride (see also Penicillin procaine and Ecmonovocillin). Solutions must be prepared aseptically. The drug is dissolved in the original vial adding the necessary amount of solvent by means of a sterile syringe passing the needle through the rubber stopper of the vial after first swabbing it with alcohol. Solutions are usually prepared with a content of 50 000—100 000 units per *ml*. Before preparing the solution the expiration date on the label is checked to see that the preparation is still fit for use. Penicillin solutions must not be warmed and they must not be mixed with acids, alkalis, alcohols or oxidizing agents (hydrogen peroxide, potassium permanganate, iodine etc.).

Note. Solutions of penicillin in procaine hydrochloride solution sometimes become turbid due to the precipitation of the procaine salt of penicillin. This is not a contraindication to the use of the solution. In such cases the solubility of the original preparation of the given lot in twice distilled water or isotonic saline should be tested. If the preparation does not dissolve freely it is unfit for use.

Doses of penicillin are individualized depending on the character of the disease, the patient's age, the effectiveness of treatment etc. The single dose for adults ranges from 50 000 to 200 000 units; the daily dose from 200 000 to 1 000 000 units. In some cases e.g. in subacute septic endocarditis massive doses are used—up to 1 500 000—2 000 000 units per day. Children up to 1 year old are prescribed 10 000—20 000 units per *kg* body weight daily; older children 150 000—400 000 units daily.

Maximal doses intramuscularly and subcutaneously for adults: single—400 000 units daily—1 200 000 units.

Maximal daily doses for children: up to 2 years old—30 000 units per *kg* body weight; from 2 to 6 years—250 000 units; 7—14 years—500 000 units.

The length of treatment depends on the character and course of the disease and may range from a few days (4—8 days in erysipelas, scarlatina, pneumonia etc.) to a month or more (for example 2—4 months in septic endocarditis). In gonorrhea without complications treatment is for 1 day 50 000—100 000 units every 3 hrs; a total of 4—8 injections or 400 000—600 000 units for the course.

Intramuscular injections of penicillin are given every 3—4 hrs if special agents are not used to prolong the effect. Solutions of penicillin in procaine hydrochloride (100 000—200 000 units of penicillin in 1 *ml* 0.25, 0.5 or 1% procaine hydrochloride solution) are injected intramuscularly up to 5 times in 24 hrs. Penicillin can be used in combination with other antibiotics and with sulfamidamide drugs. Combined therapy can promote higher effectiveness of the drugs, prevent the development of resistant forms of bacteria and so on. At the same time an aggravation of side effects is possible. Solutions of crystalline benzylpenicillin sodium are administered endolumbarly in inflammatory diseases of the brain and spinal cord and the meninges and in inflammatory processes after injuries to and operations on the central nervous system.

The dose for endolumbar injections ranges from 10 000 to 100 000 units once in 24 hrs depending on the character of the disease and the patient's age. Daily doses for children: up to 1 year old—10 000 units; from 1 to 2 years—15 000—20 000 units; from 2 to 3 years—20 000—30 000 units; from 4 to 8 years—30 000—40 000 units; over 8 years—40 000—50 000 units. Adults are

given a daily dose of 50 000 70 000 or a maximum of 100 000 units. The penicillin is dissolved in 3—10 ml of sterile twice distilled water or isotonic saline the amount depending on the amount of penicillin. When the volume of the solution is small (3—4 ml) an additional 3—4 ml of spinal fluid is drawn into the syringe. Before injecting the solution 5—10 ml spinal fluid is removed. The solution is injected slowly over a period of 1—2 min. Simultaneously with endolumbar administration of penicillin intramuscular injections are given in the usual doses. Endolumbar injections are contraindicated in epilepsy and heightened sensitivity to penicillin. In order to determine the patient's sensitivity it is advisable to inject 100 000 units of penicillin intramuscularly 12—24 hrs before endolumbar administration.

Eye drops containing 10 000—20 000 units of penicillin per ml isotonic saline are often used in ocular diseases (acute conjunctivitis corneal ulcer gonoblenorrhea etc.) 1—2 drops are instilled 6—8 times a day.

Aerosols of penicillin are often used in diseases of the lungs (chronic bronchitis pneumonia gangrene etc.) the liquid or dry aerosol is introduced into the respiratory passages by means of special atomizers at the rate of 150 000—200 000 units per inhalation twice a day.

Penicillin can likewise be administered intratracheally through a rubber catheter using the same dose dissolved in 2—3 ml isotonic saline.

In peritonitis and suppurative pleuritis penicillin solution is instilled into the abdominal or pleural cavity 100 000—200 000 units per day streptomycin is often administered simultaneously.

In inflammatory diseases of the upper respiratory passages tablets are also used these are held in the mouth until dissolved.

Treatment with penicillin and preparations containing penicillin should only be carried out on a physician's prescription and under his observation. Penicillin is only prescribed in diseases caused by penicillin sensitive microorganisms. It must be borne in mind that penicillin may have serious side effects. In some cases particularly in persons with a heightened sensitivity to the drug there is headache elevated temperature and dermatitis of varying intensity—from mild erythema to exfoliative dermatitis. Cases have been reported in the literature when the administration of penicillin caused anaphylactic shock with fatal outcome. When penicillin tablets are sucked a characteristic exfoliative glossitis occurs quite frequently when penicillin is inhaled pharyngitis and laryngitis of an allergic character may ensue as well as attacks of bronchial asthma. Side effects usually pass away of themselves when the drug is withdrawn. In severe allergic reactions adrenalin is administered. Dimedrol can also be given (doses of 0.03—0.05 g twice a day) and likewise promethazine diazolin or calcium preparations.

The temperature sometimes rises when penicillin solutions are administered parenterally in rare cases thrombosis occurs at the site of intravenous injections. Great caution is required when making injections into the spinal canal in rare cases convulsions develop in children.

When using penicillin it must be remembered that administering the antibiotic in insufficient doses as well as stopping treatment too soon may lead to the appearance of resistant strains of the causative organism.

Available in glass vials hermetically closed with rubber stoppers supplied with metal caps containing 100 000 200 000 300 000 400 000 500 000 and 1 000 000 units.

To be stored at a temperature not higher than 20°.

Solutions prepared for injection should be used immediately they can be kept for a maximum of 1—2 days if stored in a cool dark place observing all rules to maintain asepsis.

Rp Penicillin natrii (s. kalii) 200 000 units D t d N 6 in amp
S 200 000 units intramuscularly 3—4 times a day dissolve immediately before use in 1 ml 0.25% procaine chloride solution

Rp Penicillin natrii 100 000 Sol Natrii chlorati isotonicæ steril 50

MDS Eye drops 2 drops 5—6 times a day

Penicillin Ecmolin tablets to be sucked Contain 5 000 units of penicillin

Penicillin Ecmolin tablets for oral administration Contain 50 000 units of penicillin Used in angina scarlatina pneumonia and furunculosis in a dosage of 100 000 units for adults and 25 000—50 000 units for children 4—6 times a day

BENZYL PENICILLIN PROCAINE (Procaini benzylpenicillinum)

Fine crystalline powder forms fine suspension in water

Administered only intramuscularly Absorbed more slowly than the sodium or potassium salt ensures a therapeutic concentration of penicillin in the blood for a lengthy period

Indications for use are the same as for penicillin Adults are given injections of 300 000 units once a day or twice in 3 days depending on the severity of the disease The single dose for children is 5 000 units per kg body weight

Suspensions for injection are prepared immediately before use by means of a sterile syringe 2 ml sterile twice distilled water or isotonic saline is added to the vial containing the dry benzylpenicillin procaine and shaken vigorously the resulting suspension is quickly drawn into the syringe and injected deep into the muscle of the upper outer quadrant of the buttocks A thick needle is used and the syringe is washed immediately after making the injection

Available in hermetically closed vials containing 300 000 and 600 000 units

To be stored in hermetically closed vials at room temperature observing safety precautions (List B)

ECMONOVOCILLIN (Ecmonovocillinum)

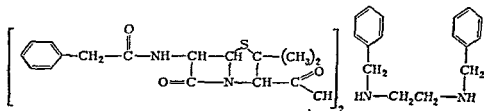
Suspension of benzylpenicillin procaine in an aqueous solution of ecmolin (Ecmonovocillin 1) or the same suspension with the addition of 100 000 units of benzylpenicillin sodium or potassium to each 300 000 units of the procaine salt (Ecmonovocillin 2) Prepared immediately before use by mixing the two ingredients 1) 300 000 or 600 000 units of benzylpenicillin procaine (or 300 000 units of benzylpenicillin procaine and 100 000 units of the sodium or potassium salt) and 2) 2.5 or 5 ml of aqueous ecmolin solution

Indications for use are the same as for penicillin Injections are given once a day

Suspensions are prepared as follows after sterilizing the needle and syringe and cleaning the needle with a mandrin the rubber stoppers of the vials are swabbed with alcohol and the needle passed through the stopper of the vial containing the ecmolin 2.5—5 ml is drawn into the syringe and transferred to the vial containing penicillin procaine or mixture of penicillin procaine and the sodium or potassium salt The mixture is carefully shaken thus forming a milky white homogeneous suspension This is immediately injected into the upper outer quadrant of the buttocks Adults are given 300 000—600 000 units daily children — 100 000—300 000 units (10 000—15 000 per kg body weight) Dispensed at the chemist's shop in two vials one containing penicillin procaine or penicillin procaine and the sodium or potassium salt the other containing ecmolin solution

BICILLIN (Bicillinum)

Crystalline salt of the benzylpenicillin and N N — dibenzylethylenediamine (Bicillin 1)



Synonyms Benzathine penicillin Benzethacil Diaminpenicillin Duapen Duropenin Penadur Penidural, Tardocillin

Fine white powder, odourless and tasteless very sparingly soluble in water (0.015% at room temperature) soluble in alcohol and acetone Forms a fine stable suspension with water

When administered intramuscularly, bicillin emulsion is slowly absorbed entering the blood over a lengthy period

Used in infectious diseases caused by organisms sensitive to penicillin Administered only Intramuscularly

When it is necessary quickly to achieve a high concentration of penicillin in the blood benzylpenicillin sodium or potassium should be administered simultaneously with bicillin For convenience in use vials are available containing a mixture of 100 000 units benzylpenicillin potassium and 300 000 units of bicillin (Bicillin 2)

Bicillin 3 is a mixture of 100 000 units each of the potassium procaine and ethylenediamine salts of benzylpenicillin (a total of 300 000 units) The preparation ensures the rapid build up of a high concentration of penicillin in the blood and its lengthy maintenance after a single administration

Such mixtures as Bicillin 2 and Bicillin-3 can also be prepared ex tempore

Bicillin suspensions are prepared aseptically before use 2 ml sterile distilled water is added to the vial containing the bicillin and the contents shaken until a homogeneous suspension is formed this is injected deep in the upper, outer quadrant of the buttocks Before making the injection one must satisfy oneself that the needle has not entered a vein

Bicillin-1 is administered to adults in a dose of 300 000 or 600 000 units once a week or 1 200 000 units once in 2 weeks children are given 5 000—10 000 units per kg body weight once a week or 20 000 units per kg body weight once in 2 weeks In treating syphilis Bicillin 1 is administered according to special instructions

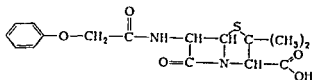
Bicillin 2 is administered to adults in a dose of 400 000—800 000 units (combined activity of 2 ingredients) once a week, or 1 600 000 units once in 2 weeks children are given 7 500—15 000 units per kg body weight once a week or 26 000 units per kg body weight once in 2 weeks More frequent injections are contraindicated

Bicillin 3 is administered to adults in a dose of 300 000 units once in 3 days or in a dose of 600 000 units once in 6 days

Available in vials containing 300 000 600 000 or 1 200 000 units calculated as benzylpenicillin. An ampoule of sterile distilled water for preparing the suspension is supplied with each vial of bicillin

To be stored at a temperature not higher than 20°

PHENOXYMETHYLPENICILLIN (Phenoxy methylpenicillinum)



Synonyms Penicillin V V Cilin

White crystalline powder very sparingly soluble in water 1 mg contains 1 600 units

Differs from benzylpenicillin in chemical structure in having a phenoxy methyl group in its molecule instead of a benzyl group. In its properties it is distinguished from benzylpenicillin by its high acid resistance, which makes it suitable for administration by mouth It is not destroyed by the acid of the

gastric juice it is absorbed well and gives a high and more prolonged concentration in the blood

Used in the treatment of infectious diseases caused by penicillin sensitive microorganism. In severe forms of disease it is advisable to begin with the intramuscular administration of benzylpenicillin after which or simultaneously phenoxymethylpenicillin is given orally

The average dose of phenoxymethylpenicillin for adults is 200 000 units 4–5 times a day. Doses for children depend on the character and severity of the disease they are usually $\frac{1}{4}$, $\frac{1}{2}$ or $\frac{3}{4}$ the dose for adults. To be taken in tablets $\frac{1}{2}$ –1 hr before meals and drunk down with water

Maximal doses for adults single—400 000 units daily—1,200 000 units

Maximal doses for children up to 3 years old single—25 000 units per kg body weight (once a day) 3–4 years single—125 000—150 000 units daily—250 000—300 000 units 5–6 years single—150 000—200 000 units daily—300 000—400 000 units 7–9 years single—250 000 units daily—500 000 units 10–14 years single—250 000—300 000 units daily—500 000—600 000 units

Treatment with phenoxymethylpenicillin should only be carried out on a physician's prescription and under his control

Like benzylpenicillin phenoxymethylpenicillin may cause various side effects including pharyngitis stomatitis and other allergic reactions as well as disorders of the gastrointestinal tract (diarrhea and vomiting) etc

Available in tablets or dragees of 100 000 and 200 000 units

To be stored at a temperature not higher than 20° observing safety precautions (List B)

ERYTHROMYCIN (Erythromycinum)

Antibacterial substance produced by *Actinomyces erythreus*

Synonym *Ilotycin*

White crystalline substance odourless bitter taste sparingly soluble in water, freely soluble in alcohol chloroform and ether. The biological potency is expressed in units of activity or in weight 1 mg = 1000 units

Erythromycin acts on gram positive microbes (streptococci pneumococci staphylococci) it is effective against microorganisms resistant to penicillin and other antibiotics

Use pneumonia pneumopleuritis scarlatina erysipelas sepsis suppurative otitis angina tonsillitis laryngitis carbunculosis wound infections and other diseases. Can be used when there is heightened sensitivity to penicillin

Erythromycin is taken orally every 4–6 hrs during meals. Single doses for adults 100 000–250 000 units in severe cases—500 000 units. Daily doses for adults 1 000 000–1 500 000 or a maximum of 2 000 000 units (2 g)

Children are prescribed 5 000–8 000 units (5–8 mg) per kg body weight every 4–6 hrs

Side effects occur relatively rarely for the most part they take the form of nausea vomiting diarrhea and lassitude. In isolated cases heightened sensitivity to the drug may be encountered. Treatment should be carried out under the observation of a physician

Available in tablets of 100 000 and 250 000 units tablets contain a filler which protects erythromycin from decomposition in the acid medium of the stomach

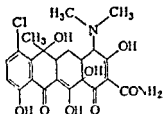
To be stored in a place protected from light at a temperature not higher than 20° observing safety precautions (List B)

BIOMYCIN HYDROCHLORIDE CHLORTETRACYCLIN HYDROCHLORIDE (*Biomycinum hydrochloricum Chlortetracyclinum hydrochloricum crystallisatum Chlortetracyclini hydrochloridum*)

Antibiotic produced by growth of the microorganism *Actinomyces aureofaciens*

Synonyms *Aureomycin Aureomykoin Duomycin*

Chemically biomycin belongs to the group of tetracyclins which also include terramycin or hydroxytetracyclin and tetracyclin



Biomycin (Chlortetracycline)

Yellow crystalline powder odourless bitter taste very sparingly soluble in water (1.3% at 18°). Solutions are yellow pH = 2.7—2.9. Stable in weakly acid medium. Easily decomposes in strong acids and alkalis. Slowly decomposes in light stable in air.

The potency of biomycin (chlortetracycline) is expressed in weight or units of activity. One unit is equal in activity to one microgram of chemically pure chlortetracycline hydrochloride.

Biomycin has a broad antibacterial spectrum. Effective against gram positive and gram negative microbes, rickettsiae and some viruses.

Use: bacterial pneumonia, dysentery, brucellosis, tularemia, whooping cough, gonorrhea and some other bacterial infections as well as typhus and other rickettsioses and amoebic dysentery. Effective in trachoma, psittacosis and some other diseases caused by large viruses.

Also used for the prevention and treatment of infectious complications in surgical patients, particularly in operations in the abdominal cavity, used in peritonitis caused by intestinal microorganisms, surgical sepsis and suppurative diseases of the lungs.

Applied locally in the treatment of patients with burns, phlegmons, mastitis, abscesses (by instilling an aqueous solution of biomycin into the abscess cavity after first removing the pus by aspiration), purulent skin diseases, conjunctivitis, blepharitis, trachoma and other infectious ocular diseases.

Biomycin has a good effect in infections of the genitourinary system as well as in infectious diseases caused by microbes resistant to penicillin and streptomycin.

Biomycin is ineffective in poliomyelitis, botulism and infections caused by *Proteus*, *Pseudomonas pyocyanea* and yeasts.

In severe septic conditions, pneumonia and other diseases, biomycin can be used in combination with other antibiotics and sulfanilamide drugs.

Administered by mouth half an hour before meals in the form of tablets or capsules to be drunk down with water.

Single dose for adults 0.1—0.2 g (100,000—200,000 units), usually given 5—6 times a day. Course of treatment 6, 8 or 10 days, if necessary treatment is repeated after a break of 6, 10 or 15 days. Children are prescribed biomycin at the rate of 0.025 g (25,000 units) per kg body weight daily.

In treating gonorrhea, adults are given 0.3 g 4—5 times a day, total dose for the course—4—5 g (400,000—500,000 units).

In treating acute dysentery in adults, biomycin is administered orally alone or in combination with other drugs according to one of the following schedules:

Biomycin

1st, 2nd, 3rd and 4th day 0.4 g (400,000 units) biomycin 4 times a day
5th, 6th and 7th day 0.3 g (300,000 units) biomycin 4 times a day

Biomycin with phthalazol (or sulgin)

1st and 2nd day 0.4 g biomycin and 1 g phthalazol 4 times a day
3rd to 5th " 0.3 g " " 1 g " 4 " " "
6th and 7th " 0.2 g " " 1 g " 4 " " "

Biomycin with streptomycin and ecmolin

0.4 g biomycin and 120 000 units of streptomycin dissolved in 5 ml 0.5% solution of ecmolin 4 times a day for 5–7 days

To prevent early relapses a second course is given after 3–5 day break the dosage and length of treatment being the same as those specified above

In treating chronic dysentery and bacilli carriers administration of biomycin can be combined with vaccinothérapie

Maximal doses for adults single—0.5 g daily—2 g

Maximal doses for children up to 5 years old—0.025 g (25 000 units) per kg body weight daily 5–6 years single—0.1 g daily—0.4 g 7–9 years single—0.15 g daily—0.6 g 10–14 years single 0.2–0.3 g daily—0.8–1 g

Aqueous solutions of biomycin for local application are prepared ex tempore at the rate of 1–5 mg in 1 ml 0.5–1% ointments are also used locally

Reports have been published on the administration of biomycin intramuscularly Children were administered 25–5 mg per kg body weight daily in 2 injections The single dose was injected in 1 ml 0.25–0.5% procaine hydrochloride and 1 ml 0.5% ecmolin solution (Z. V. Yermolyeva et al) Intramuscular injections are painful

Biomycin should only be used on a physician's prescription and under his observation

Biomycin like other broad spectrum antibiotics may relatively often cause side effects When taking biomycin there may be poor appetite nausea vomiting intestinal disorders (loose stool) hyperemia of the mucous membranes of the mouth and pharynx dermatitis accompanied by pruritus Quincke's edema and other allergic reactions

Lengthy use of biomycin may give rise to affections of the skin and the mucous membranes of the gastrointestinal tract vagina lungs and other organs caused by the yeastlike fungus *Candida albicans* (candidamycoses) fungous septicemia may also occur

Candidamycoses may also develop when other antibiotics are used (terramycin levomycetin synthomycin etc) especially if they are used in combination *Candida albicans* is found in the normal microflora of the skin and mucosa being a saprophyte under usual conditions By suppressing the usual microflora antibiotics foster the growth of the fungus and its transition to a parasitic condition—something that may lead to severe complications It is possible that disturbance of the formation of vitamins by the normal microflora of the body and changes in the body's resistance may also be conducive to the development of candidamycoses

Special antifungous antibiotics are now being used for the treatment of candidamycosis (see Nystatin)

During treatment with biomycin careful watch must be kept on the patient's condition if there should be symptoms of heightened sensitivity to the antibiotic or side effects a break should be made in treatment or biomycin with drawn or replaced by another antibacterial drug if necessary nystatin is prescribed

Biomycin is contraindicated in cases of heightened sensitivity and impairment of the function of the liver as well as in the presence of fungous diseases caution is necessary in leukopenia

Available in powder form and in tablets of 0.1 g

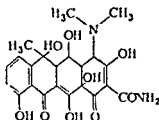
To be stored in a dry place protected from light at room temperature (no higher than 20°) observing safety precautions (List B)

Rp Biomycini (s Chlorotetracyclini) hydrochlorici 100 000 units
 D t d N 20 in tabul
 S 2 tablets 5 times a day

Rp Biomycini hydrochlorici 01 (100 000 units)
 Aq destill 200
 MDS Lotion (to be prepared ex tempore!)

HYDROXYTETRACYCLIN, Terramycin (Hydroxytetracyclinum, Terra mycinum)

Antibiotic produced by growth of the microorganism *Actinomyces rimosus*
 Synonyms Oxymykoln Oxyterracyna Oxytetracyclin Tetran
 Closely related to tetracyclin and biomycin in action and structure



Terramycin (Hydroxytetracyclin)

Hydroxytetracyclin base greyish yellow powder, bitter taste sparingly soluble in water Hydrochloride yellow crystalline powder soluble in water and alcohol

The potency of hydroxytetracyclin is expressed in weight or units of activity 1 mg contains 1 000 units 1 unit—1 µg

In its antibacterial spectrum hydroxytetracyclin is similar to biomycin It is quickly absorbed and remains in the body for a relatively long period

Use pneumonia bacillary and amoebic dysentery whooping cough gonorrhea brucellosis typhus psittacosis infectious diseases of the genitourinary system infectious complications in surgical patients ocular diseases (conjunctivitis blepharitis etc) otorhinolaryngology (tonsillitis otitis mastoiditis etc) and other infectious diseases Effective in diseases caused by organisms resistant to penicillin and streptomycin

Administered orally and intramuscularly

Orally hydroxytetracyclin is given in tablets Dosage for adults 100 000—500 000 units (01—05 g) 3—4 times a day The course of treatment is for 4—10 days Oral dose for children up to 3 years old—0025 g (25 000 units) per kg body weight daily over 3 years old—0075 01 or 02 g 3—4 times a day

Maximal doses for adults orally single—05 g daily—2 g

Maximal doses for children up to 5 years old—25 000 units (0025 g) per kg body weight daily 5—6 years single—02 g daily—04 g 7—9 years single—02—025 g daily—04—05 g 10—14 years single—025—03 g daily—05—06 g

Hydroxytetracyclin is more effective when administered intramuscularly than when taken orally Intramuscular injections are used in severe courses of infectious diseases especially in children as well as in cases where oral administration is difficult or impossible (because of vomiting diarrhea operations in the oral cavity and on the gastrointestinal tract or unconscious condition of the patient etc)

For intramuscular administration a solution of hydroxytetracyclin in a solution of procaine hydrochloride or procaine hydrochloride and ecmolol is used

The contents of 1 vial of hydroxytetracyclin hydrochloride (100 000 units) are dissolved in 5 ml 1–2% procaine hydrochloride solution or in 2.5 ml procaine and 2.5 ml 0.5% emolin solution and the contents of the vial thoroughly shaken the resulting solution or fine homogeneous suspension is injected in the upper outer quadrant of the buttocks Intravenous injection is not permissible The single dose for adults is 40 000–60 000 units (2–3 ml of solution) Doses for children up to 1 year old—10 000 units (0.5 ml) from 1 to 5 years—20 000 units (1 ml) over 5 years—30 000–40 000 units (1.5–2 ml) Injections can be given 2–3 times in 24 hrs Average length of course of treatment—5–10 days if necessary 2–3 cycles of treatment are given with breaks of 4–7 days

Intramuscular injections of hydroxytetracyclin hydrochloride may be painful if there should be great pain and persistent infiltrates should appear at the injection site injections are discontinued

Hydroxytetracyclin hydrochloride can also be used for instillation into the abdominal and pleural cavities or for injection into the joints in affections caused by microbes sensitive to hydroxytetracyclin The same solution is used as for intramuscular administration the single dose for instillation into cavities is 20 000–80 000 units

An ointment containing 10 000 (or 5 000) units hydroxytetracyclin per g is available for the treatment of ocular diseases (conjunctivitis blepharitis keratitis trachoma and other infectious diseases caused by hydroxytetracyclin sensitive organisms)

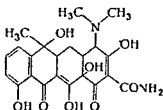
The ointment is applied under the lower lid 3–5 times a day

Possible complications and contraindications are the same as for biomycin

Available in powder form in tablets of 0.1 and 0.2 g in vials containing 0.1 g and in the form of 0.5% and 1% ointment

To be stored at room temperature (not higher than 20°) Solutions may be kept in refrigerator for a maximum of 24 hrs

TETRACYCLIN (Tetracyclinum)



Synonyms Achromycin Cyclomycin Deschloraureomycin Deschlorbiomycin Hostacyclin Panmycin Polycycline Steclin Tetrabon Tetracyn

Tetracyclin base light yellow crystalline powder odourless and tasteless sparingly soluble in water and organic solvents Tetracyclin hydrochloride is soluble in water at room temperature (0.7%)

Similar in chemotherapeutic activity to biomycin and terramycin Tolerated relatively well convenient for use in pediatric practice because it has no bitter taste Maintained in higher concentrations in the blood than other antibiotics of the tetracyclin group

Used for the treatment of pneumonia subacute septic endocarditis bacillary and amoebic dysentery whooping cough gonorrhea brucellosis tularemia typhus psittacosis and infectious diseases of the urinary tract also used to prevent infectious complications in surgical patients

Applied locally in burns phlegmons and mastitis

In severe septic diseases tetracyclin can be used in combination with penicillin and streptomycin

Tetracyclin base is administered by mouth half an hour before or an hour after meals. Taken in the form of tablets, wafers or capsules containing 0.1—0.15 g (100 000—150 000 units) 4—6 times a day.

Maximal daily dose for adults—2 g

Children up to 3 years old are prescribed tetracyclin orally at the rate of 0.025 g (25 mg) per kg body weight daily (in 4 doses); children over 3 years old are prescribed 0.075—0.1 g 3—4 times a day.

The course of treatment averages 7—8 days.

Tetracyclin hydrochloride is applied locally in the form of ointments (1—2%) and eye drops (0.5%). Solutions are prepared immediately before use; they cannot be kept for more than 24 hrs. Solutions of tetracyclin hydrochloride can also be used for intramuscular injections and instillation into cavities (see Hydroxytetracyclin).

Tetracyclin base is available in powder form and in tablets. Tetracyclin hydrochloride is available in the form of 1% and 2% ointments prepared with a special emulsifier.

Ointments can be kept in the refrigerator 4 months.

Rp Tetracyclini 0.15

D t d N 20 in tabul

S 1 tablet 4—6 times a day

Rp Ung Tetracyclini hydrochlorici 1% 100

DS Eye ointment

COLIMYCIN (Colimycinum)

Antibiotic substance of the neomycin group obtained from the culture medium of the filamentous fungus *Streptomyces fradiae* var *spiralis*.

White powder or white or cream coloured porous mass, faint characteristic odour, saline taste, soluble in water, insoluble in alcohol.

The unity of activity is 1 µg colimycin base.

Colimycin has a broad spectrum of action. It inhibits the growth of gram positive microbes (staphylococci, streptococci, pneumococci) and gram positive bacteria (dysentery bacilli, coli bacilli, *Proteus*, *Fründliners* bacillus and to a lesser extent *Pseudomonas pyocyanea*).

Use: pyodermitis, various skin diseases complicated with staphylo and streptoderma, suppurative processes in the abdominal and pleural cavities, wounds of the soft tissues infected with microbes sensitive to the antibiotic. Colimycin is used orally in children for the treatment of enteritis caused by coli bacilli; it is not however effective in dysentery.

In affections of the soft tissues, tampons are used moistened with 0.25—0.5% colimycin solution in 0.5% solution of procaine hydrochloride. Tampons are changed every day for 5—7 days. In osteomyelitis, colimycin is instilled into the cavity after the operation. A dose of 200 000 units of colimycin is used while the amount of solvent (water or 0.5% procaine hydrochloride solution) depends on the size of the cavity. Instilled 2—3 times over a period of 7—10 days. In suppurative processes in the abdominal cavity, 700 000—1 400 000 units of colimycin dissolved in 0.5% procaine hydrochloride solution are instilled (5—10 ml procaine hydrochloride solution per 35 000 units). In order to prevent suppurative complications, 700 000 units of colimycin dissolved in 10—20 ml 0.5% procaine is instilled into the abdominal cavity. In pleural empyema, the cavity is washed with colimycin dissolved in 0.25—0.5% procaine hydrochloride solution at the rate of 350 units per ml. After lavage, 300 000—700 000 units of colimycin dissolved in 20 ml 0.5% procaine is instilled into the cavity.

In dermatological practice, a 5% ointment or colimycin lotions are used.

Hemorrhoidal suppositories containing colimycin have also been proposed.

[Antiseptic biological suppositories]

When colimycin is applied locally there may be irritation in the skin at the focus of affection and in the surrounding healthy skin. If the skin should be irritated application of colimycin should temporarily be stopped.

Contraindications to the use of colimycin ointment and aqueous solution pronounced symptoms of irritation in the skin of affected areas or in surrounding healthy skin.

In enteritis colimycin is administered orally at the rate of 20 000—50 000 units per kg body weight daily. The daily dose is given in 4 parts at intervals of 6 hrs. Course of treatment 5—7 days. When the drug is given orally side effects may occur in the form of nausea, vomiting and diarrhea.

Treatment with colimycin should be carried out under the observation of a physician. Neuritis of the auditory nerve is possible during lengthy parenteral administration and the absorption of substantial amounts of the antibiotic.

Available in ampoules or vials containing 175 000, 350 000 or 700 000 units.

To be stored in hermetically closed containers in a dry place protected from light at room temperature observing safety precautions (List B).

Aqueous solutions of colimycin can be kept for 48 hrs at a temperature of 6°. In ointments the activity of the antibiotic is maintained for 2 months.

MYCERIN (Mycerinum)

Antibiotic substance of the neomycin group.

Cream coloured powder, odourless and tasteless, soluble in water. The potency is expressed in units of activity. Mycerin has a broad spectrum of action; it is effective against gram positive and gram negative bacteria and acts on microorganisms resistant to penicillin and streptomycin. Mycerin is not effective in acute dysentery.

Administered orally and locally. The oral dose for adults is 100 000—200 000 units twice a day. Small children are given mycerin at a rate of 4 000 units per kg body weight twice a day. The course of treatment should not exceed 5—7 days. The antibiotic can be administered orally in the form of a solution containing 4 000 units per ml.

For local application (treatment of wounds, ulcers, etc.) a 1% aqueous solution of mycerin is used; the total amount of the solution for a single application should not exceed 25—50 ml and the daily amount should not exceed 50—100 ml. Ointments containing 1—2% mycerin are likewise used (for phlegmons, burns, etc.).

Treatment with mycerin should be carried out under the careful observation of a physician. Treatment should be begun with small doses of the antibiotic; the use of large doses may cause side effects: elevated temperature, chills, etc. The drug is contraindicated in diseases of the kidneys.

To be stored in hermetically closed vials at a temperature not higher than 20°, observing safety precautions (List B).

ECMOLIN (Ecmolinum)

0.5% solution of triprotamine sulphate. Has the ability to prolong and intensify the action of penicillin and other antibiotics. Has an antibacterial action on hemolytic streptococci, staphylococci, dysentery bacilli and some other microorganisms. An ingredient of ecmovocillin. Has also been proposed for the prevention and treatment of catarrhal manifestations in the upper respiratory passages during influenza. 4—6 drops are instilled into each nostril 3 times a day, also administered by inhalation or in the form of an aerosol (0.5 ml ecmolin in 5 ml isotonic saline).

Available in vials containing 10 ml.

NYSTATIN (Nystatinum)

Antibiotic substance produced by *Streptomyces noursei*.

Synonyms: Fungicidin, Fungistatin, Mycostatin.

Yellow powder, bitter taste, practically insoluble in water, sparingly soluble in alcohol, rapidly decomposes in acid and alkaline media.

The biological potency of nystatin is expressed in units of activity. 1 mg contains about 2 500 units.

Nystatin acts on pathogenic fungi particularly yeast like fungi of the genus *Candida* inactive against bacteria Nystatin is absorbed poorly most of that taken by mouth is excreted in the feces

Used for the prevention and treatment of diseases caused by yeast like fungi of the genus *Candida* (*C. albicans* etc.) Indicated for the treatment of candidamycosis of the mucous membranes (mouth vagina etc.) skin and internal organs (gastrointestinal tract lungs kidneys etc.) It is used to prevent the development of candidamycosis during lengthy treatment with antibiotics especially when antibiotics of the tetracycline series are given orally

Nystatin is administered orally in the form of tablets Adults are given 250 000—500 000 units 3—4 times a day or 250 000 units 6—8 times a day; in severe cases of visceral candidamycosis or candidasepsis 500 000 units is prescribed 6—8 times a day Doses for children up to 1 year old — 75 000 units from 1 to 3 years — 100 000 units 3—4 times a day over 3 years old — 500 000—750 000 units a day (in 4 doses) Average course of treatment 10—14 days Treatment is repeated in cases of chronic relapsing and generalized candidamycosis

In treating fungous affections of the mucous membranes and skin ointments emulsions and suspensions containing 100 000 units nystatin per g or per ml can also be used

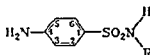
Nystatin is only slightly toxic, and usually causes no side effects When there is heightened sensitivity to the antibiotic nausea vomiting diarrhea elevated temperature chills etc. may occur in such cases the dose is reduced

Available in dragees each containing 100 000—250 000 or 500 000 units Compound tablets are also available containing nystatin and biomycin or hydroxytetracycline (100 000 units of each antibiotic)

To be stored in a dry place protected from light at a temperature not higher than 20°

B Sulfanilamide drugs

The sulfanilamide drugs comprise a large group of compounds with the general formula



One of the atoms of hydrogen of the amino group at position 4 can also be replaced by various radicals

Drugs of this group are active antimicrobial agents Their antimicrobial effect results for the most part from impairment of the microbes ability to synthesize the essential "growth factors" — folic acid and other substances whose molecules contain para aminobenzoic acid (see Procaine hydrochloride) The sulfanilamides are closely related in chemical structure to para aminobenzoic acid and block the biochemical systems whose function it is to bind para aminobenzoic acid in this way they disturb the course of metabolic processes and stop the growth and reproduction of the microbes In order to achieve a therapeutic effect sulfanilamides must be administered in large doses sufficient to prevent the microbes from utilizing the para aminobenzoic acid contained in the tissues The administration of sulfanilamide drugs in insufficient doses or the stopping of treatment too soon may lead to the development of resistant strains of the causative organisms Another circumstance that must be taken into account is that some drugs whose molecules contain a para aminobenzoic acid residue for example procaine may have a marked antisulfanilamide effect

A variety of sulfanilamide drugs are being used in medical practice today The choice of drug depends on the causative organism and the course of the

disease the pharmacological properties of the drug and the extent to which it is tolerated etc Factors of importance are the absorbability of the drug from the gastrointestinal tract the ways and speed of excretion and the ability to penetrate into different organs and tissues Sulfanilamide norsulfazol the group of pyrimidine derivatives (sulfadimezine etc) and ethazol are absorbed relatively rapidly and are chiefly excreted through the kidneys Urosulfan is also absorbed readily and largely excreted in the urine Other drugs like phthalazol and sulgin are poorly absorbed from the gastrointestinal tract remain in the intestine in high concentrations for relatively long periods and are mostly excreted in the feces

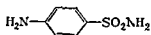
Sulfanilamide drugs can be used in various combinations this often heightens their effectiveness and in some cases reduces their toxicity (as for example in the combined use of pyrimidine derivatives) It is an advantage to combine drugs that are poorly absorbed with those that are absorbed well Sulfanilamides are often prescribed in conjunction with antibiotics (see Levomycetin Biomycin etc.)

Sulfanilamide drugs can cause allergic and other side effects nausea vomiting dermatitis leukopenia neuritis etc Changes in the central nervous system (psychoses) sometimes occur pyrimidine derivatives fairly frequently cause impairment of the function of the kidneys

Because of the possibility of side effects and the development of sulfanilamide resistant microorganisms patients should be warned that these drugs should only be taken when prescribed by a physician

SULFANILAMIDE (Sulfanilamidum)

p Aminobenzenesulfonamide



Synonyms Ambesid Consulanid Deseptyl Dipron Gombardol Lysococcine, Pabiamid Prontalbin Prontalin Prontoin Proseptine Proseptol Stramid Streptocid Streptozol Sulfamidyl Sulfanilamid

White of slightly yellowish crystalline powder odourless sparingly soluble in water (1:170) freely soluble in boiling water sparingly soluble in alcohol (1:35) practically insoluble in ether and chloroform freely soluble in dilute hydrochloric acid soluble in solutions of caustic alkalis Aqueous solutions are neutral Melting point 164–167° Solutions are sterilized by holding at 100° for 30 min

Sulfanilamide was one of the first chemotherapeutic drugs of the sulfanilamide group When it comes to chemical structure other drugs of this group can be considered derivatives Sulfanilamide has a marked antimicrobial action against streptococci meningococci gonococci pneumococci coli bacilli and some other bacteria

Used for the treatment of epidemic cerebrospinal meningitis erysipelas angina and other coccal infections acute and chronic gonorrhea and colibacillosis (cystitis pyelitis colitis) as well as for the prevention of wound infection and suppurative complications in operations and for the treatment of infected wounds and fractures

Administered orally Dose for adults 0.5–1 g 5–6 times a day 3–6 g in 24 hrs Doses for children up to 1 year old — 0.05–0.1 g from 2 to 5 years — 0.2–0.3 g from 6 to 12 years — 0.3–0.5 g

In cases of persistent vomiting and when the patient is unconscious oral administration of sulfanilamide can be replaced by subcutaneous or intravenous administration of soluble sulfanilamide

In the treatment of gonorrhea sulfanilamide is administered orally for 10 days in succession in a dosage of 3 g per day

Maximal doses for adults single — 2 g daily — 7 g

Maximal doses for children 0.2 g per kg body weight daily

Sulfanilamide is used locally for powdering or blowing into wounds 5-10 or 15 g of thoroughly powdered sulfanilamide is applied to the wound (the powder should first be sterilized) Simultaneously with local application sulfanilamide is administered orally 6-7 g the 1st day and then 5-6 g daily Local application of sulfanilamide is often combined with oral administration of norsulfazol or sulfadimezine in the doses indicated Local administration of sulfanilamide alone is not sufficiently effective

A mixture of sulfanilamide norsulfazol penicillin and ephedrine is used in acute coryza the powder is blown into the nasal cavity with a special dusting device or is drawn into the nose by inhaling

Sulfanilamide is quickly absorbed when introduced into the body The highest concentration in the blood is found in 1-2 hrs after administration In 4 hrs it is detected in the spinal fluid It is chiefly excreted by the kidneys (90-95%)

When sulfanilamide is administered headache vertigo nausea and vomiting sometimes occur there may be cyanosis

The administration of large doses may cause complications in the hemopoietic system (leukopenia agranulocytosis) Side effects are at times observed involving the nervous and cardiovascular systems (paresthesia tachycardia) as well as dermatitis and diarrhea Complications involving the urinary tract are rarely encountered

Lately sulfanilamide has been replaced to an increasing extent by sulfadiazine norsulfazol ethazol and other more effective sulfanilamide drugs which have fewer side effects

Contraindications to treatment with sulfanilamide decompensation of cardiac activity pronounced atherosclerosis severe diseases of the hemopoietic system (pernicious anemia leukemia) active tuberculosis nephrosis and nephritis exophthalmic goiter and pathological pregnancy During lengthy treatment with sulfanilamide the blood must be examined regularly as a control measure

Available in powder form and in tablets of 0.3 and 0.5 g

To be stored in glass bottles with ground glass stoppers observing safety precautions (List B)

Sulfanilamide ointment Composition sulfanilamide 1 part petrolatum 9 parts Used for the treatment of wounds ulcers burns fissures etc.

Sulfanilamide suspension. Composition sulfanilamide 5 parts glycerol 5 parts emulsifier 20 parts salicylic acid (preservative) 0.25 parts water to make 100 parts

Ointment like mass with characteristic odour

Used locally for the treatment of suppurating wounds infected burns erysipelas and other purulent inflammatory processes Applied directly to the affected surface or spread on a gauze dressing The dressing is changed in 1-2 days

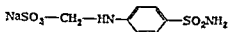
To be kept well closed at room temperature in a place protected from light

Sulfanilamide emulsion (Emulsio streptocidi 5%) Composition sulfanilamide 5 g fish liver oil 34 g emulsifier 5 g distilled water 56 g

Thick yellowish homogeneous cream like mass with odour of fish liver oil mixes with water when shaken Used in the same way as sulfanilamide suspension To be stored in tightly closed jars in a cool place protected from light. If a brownish film should appear on the surface of the emulsion during storage (oxidation product from the oil) it should be removed after which the emulsion can be used

SULFANILAMIDE SOLUBLE (Sulfanilamidum solubile)

Sodium p sulfamidophenylaminomethylenesulfonate



White crystalline powder freely soluble in water insoluble in organic solvents Solutions are sterilized by holding at 100° for 30 min pH of 10% solution = 4.0—5.0

Soluble sulfanilamide is an active chemotherapeutic agent The high solubility in water makes possible extensive use for parenteral administration Solutions can be injected subcutaneously intramuscularly and intravenously

Used in infections caused by streptococci gonococci meningococci pneumococci and coli bacilli

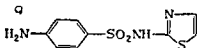
For subcutaneous and intramuscular administration a 1—15% solution prepared with distilled water or isotonic saline is used Administered in a dose of 100 ml 2—3 times a day For intravenous administration a 2.5 or 10% solution is used solutions are prepared with twice distilled water isotonic saline or 1% glucose Administered in doses of 20—30 ml

The use of soluble sulfanilamide is especially convenient in cases where the patient's condition makes oral administration impossible (vomiting unconscious state) Solutions of the drug are administered parenterally with the aim of getting the patient out of the serious condition after which sulfanilamide compounds can be given orally Soluble sulfanilamide can be administered orally as well as parenterally In this case the dosage is the same as for sulfanilamide

Available in powder form To be stored in well stoppered bottles observing safety precautions (List B)

NORSULFAZOL (Norsulfazolum)

2 (p Aminobenzenesulfonamido) thiazole



Synonyms Azoseptale Cibazol Eleudron Pyrisulfon Sulfathiazolum Sulphathiazolum Thiazamide Unozol Wintrazole

White crystalline powder odourless almost insoluble in water sparingly soluble in alcohol and acetone practically insoluble in ether soluble in dilute mineral acids and solutions of caustic alkalis and carbonates Melting point 198—203°

Norsulfazol is effective in infections caused by hemolytic streptococci pneumococci gonococci and staphylococci as well as coli bacilli

Easily absorbed from the gastrointestinal tract and rapidly excreted chiefly in the urine and for the most part in the free unacetylated form Complications involving the kidneys are rarely observed when the drug is used Nausea occurs relatively frequently and in rare cases vomiting

Used orally in pneumonia cerebrospinal meningitis gonorrhea staphylococcal and streptococcal sepsis and other infectious diseases In pneumonia and meningitis adults are given an initial dose of 2 g and then 1 g every 4—6 hrs until the temperature falls subsequently 1 g is taken every 6—8 hrs During the course of treatment the patient takes a total of 20—30 g In staphylococcal infections the initial dose is 3—4 g followed by 1.5 g every 4 hrs In gonorrhea 1 g is given 5 times a day and then 4 times a day The course of treatment is for 3—6 days In the treatment of dysentery the drug is prescribed in the same dosage as sulfadimezine

Children are given norsulfazol every 4, 6 or 8 hrs in the following doses from 4 months to 2 years old—0.1—0.25 g from 2 to 5 years—0.3—0.6 g from 6 to 12 years—0.5—0.75 g The initial dose is a double one

Maximal doses for adults single—2 g daily—7 g

Maximal daily dose for children 0.2 g per kg body weight

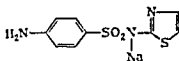
When using norsulfazol it is advisable to maintain diuresis To this end 2—3 liters of liquid should be ingested daily after each dose of the drug a glass

of water containing $\frac{1}{2}$ teaspoonful of sodium bicarbonate should be drunk or 1 glass of Borzhomi mineral water

Available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well stoppered bottles in a dry place observing safety precautions (List B)

NORSULFAZOL, SOLUBLE (Norsulfazolum solubile)



Synonyms Sulfathiazolum sodium Sulfathiazolum natrium

Lustrous colourless or slightly yellowish leaflets odourless, freely soluble in water (1/2) soluble in alcohol (1/15) Aqueous solutions are strongly alkaline Solutions are sterilized by holding at 100° for 30 min

Chemotherapeutic activity the same as that of norsulfazol Since the drug is soluble in water it can be administered parenterally as well as orally Solutions are only injected intravenously, being injected subcutaneously they cause irritation of the tissues to the extent of necrosis

Indications for use are the same as for norsulfazol Intravenous administration is resorted to when it is impossible to give norsulfazol orally, for example after operations on the gastrointestinal tract In cases of vomiting and when the patient is unconscious as well as when it is necessary quickly to build up a high concentration in the blood As soon as the patient's condition permits intravenous administration of soluble norsulfazol is discontinued in favour of oral administration of sulfanilamide drugs

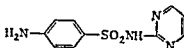
Administered intravenously in the form of 5% or 10% solutions at the rate of 0.5 l or 2 g per injection (10–20 ml of 5% or 10% solution) the injection is performed slowly

Available in powder form

To be stored in small glass bottles well stoppered and sealed with paraffin wax or in small polyethylene bags in a place protected from light observing safety precautions (List B)

SULFAZINE (Sulfazinum)

2 (p-Aminobenzenesulfonamido) pyrimidine or 2 sulfanilamidopyrimidine



Synonyms Adiazin Debenal Eustral Pharmadiazin Pyrimal Sulfadiazinum Sulfapyrimidin

White or yellowish powder odourless soluble in alcohol and acetone soluble in solutions of alkalis and mineral acids practically insoluble in water Melting point $252\text{--}256^{\circ}$

Has an antibacterial activity in infections caused by hemolytic streptococci and staphylococci pneumococci meningococci and gonococci

Sulfazine causes nausea and vomiting relatively rarely complications involving the homopoietic system are also rare but complications involving the urinary system occur at times such as hematuria oliguria and anuria

Sulfazine is slowly absorbed when administered orally The maximal concentration in the blood is reached in 3–6 hrs excreted more rapidly by the kidneys than methylsulfazine and sulfadimezine

Administered orally in powders or tablets The initial dose for adults is 2–4 g (4 g in severe infections), followed by 1 g every 4 hrs On the 4th day the dosage is reduced to 1 g every 6–8 hrs Treatment is continued till the

temperature falls and for an additional 3 days. The course of treatment is usually 5–7 days.

Children are given an initial dose of 0.1 g per kg body weight followed by 0.025 g (25 mg) per kg body weight every 4–6 hrs.

In the treatment of dysentery the dosage is the same as that for sulfadiazine.

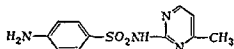
Sulfazine is often used in combination with methylsulfazine, sulfadiazine and other sulfanilamide drugs.

Diuresis must be maintained during treatment with sulfazine, the intake of large amounts of alkaline fluids can prevent complications involving the kidneys.

To be stored in well stoppered bottles observing safety precautions (List B).

METHYLSULFAZINE (Methylsulfazinum)

2 (p-Aminobenzenesulfonamido) 4-methylpyrimidine



Synonyms: Debenal M, Merazene, Methyldebenal, Methylsulfazine, Pyrimal M, Septacil, Sulfamerazinum, Sulfamethylpyrimidin, Sumedine.

Slightly cream coloured powder, insoluble in water, soluble in dilute acids and alkalis. Melting point 232–235°.

Has high activity in infections caused by hemolytic streptococci and pneumococci. Also active against meningococci and microbes of the coli group. Similar to sulfazine and sulfadiazine in character of action. Absorbed more rapidly than sulfazine, slowly excreted by the kidneys. Methylsulfazine is only slightly toxic and is usually tolerated well by patients.

Used in pneumonia, streptococcal infections and erysipelas. Also recommended in infections caused by meningococci and coli bacilli.

Administered orally in the form of powders or tablets. Doses for adults are the same as for sulfazine.

The initial dose for children is 0.1 g per kg body weight followed by 0.025 g per kg body weight every 4, 6 or 8 hrs.

Maximal doses are the same as for sulfadiazine.

It is advisable to prescribe the copious intake of alkaline fluids when administering methylsulfazine.

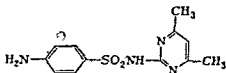
When using the drug, nausea, vomiting and skin eruptions sometimes occur and in rare cases crystals are precipitated in the urinary tract. If side effects develop the dose is reduced and if necessary administration of the drug is discontinued.

Available in powder form and in tablets of 0.5 g.

To be stored in well closed containers in a place protected from light, observing safety precautions (List B).

SULFODIMEZINE **SULFADIMEZINE** (Sulfodimezinum, Sulfadimezinum)

2 (p-Aminobenzenesulfonamido) 4,6-dimethylpyrimidine



Synonyms: Diazil, Diazol, Dimethazil, Dimethyldebenal, Dimethylsulphadiazine, Dimethylsulphapyrimidine, Purmazin, Sulfadimerazine, Sulfamézatil.

Sulfamethazine, Sulfamezatine, Sulmet, Sulphadimethylpyrimidine, Sulphadimidine Superseptil

White or slightly yellowish powder, sparingly soluble in water, freely soluble in dilute acids and alkalis Melting point 196—200°

Similar to sulfazine and methylsulfazine in antimicrobial action

Rapidly absorbed when administered orally, slowly excreted by the kidneys

Used in pneumococcal, streptococcal and meningococcal infections, as well as in infections caused by coli bacilli and other microbes The drug is especially indicated in severe pneumococcal infections and in infections of the urinary tract

Administered orally in the form of powders or tablets Doses for adults and children are the same as for methylsulfazine

Maximal doses for adults single—2 g. daily—7 g

Maximal daily dose for children 0.2 g per kg body weight

When treating dysentery, sulfadimezine is prescribed for adults according to the following schedule 1st and 2nd day of the disease—6 g in 24 hrs (1 g every 4 hrs), 3rd and 4th day—4 g in 24 hrs (1 g every 6 hrs) 5th and 6th day—3 g in 24 hrs (1 g every 8 hrs) Total drug for the course of treatment 25—30 g After a 5—6 day break a second cycle of treatment is carried out 1st and 2nd day—1 g every 4 hrs (every 8 hrs at night) a total of 5 g in 24 hrs 3rd and 4th day—1 g every 1 hrs (not administered at night), a total of 4 g in 24 hrs 5th day—1 g every 4 hrs (not administered at night), a total of 3 g in 24 hrs Total drug for second cycle 21 g (in mild cases the total dose can be reduced to 18 g)

When treating dysentery in children, the following doses are prescribed up to 3 years old—daily dose of 0.2 g per kg body weight (given in 4 portions during daytime without disturbing night sleep) The drug is given in this dosage for 7 days Children over 3 years old are given doses of 0.4—0.75 g 4 times a day the size of the dose depending on the age

Sulfadimezine can be used in combination with levomycelin, synthomycin and other antibiotics

The copious intake of alkaline fluids should be prescribed during treatment with sulfadimezine Morphological examination of the blood must be carried out regularly the same as during treatment with other sulfanilamide drugs

Available in powder form and in tablets of 0.25 and 0.5 g

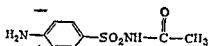
To be stored in well stoppered bottles in a dry place, observing safety precautions (List B)

Rp Sulfadimezini 0.5
D t d N 24 in tabul
S 2 tablets 4—6 times a day

Rp Sulfadimezini 0.5
Sulfazini
Methylsulfazini 5ā 0.25
M f pulv D t d N 24
S 1 powder 6 times a day

SULFACYL (Sulfacylum)

Sulfanilacetamide p aminobenzenesulfonacetamide



Synonyms Acetocid Acetosulfamin, Albucid, Alesten, Septuron, Steramid, Sulamid Sulfacetamidum, Sulphasil, Urosulfon

White or slightly yellowish crystalline powder odourless soluble in 200 parts cold water readily soluble in hot water soluble in 12 parts alcohol soluble in mineral acids and solutions of caustic alkalis Melting point 178—181°

Effective in streptococcal gonococcal pneumococcal and coli bacillary infections

Administered orally in pyelitis cystitis mastoiditis puerperal sepsis enterocolitis and other infectious diseases

Applied locally as a dusting powder in the treatment of infected wounds

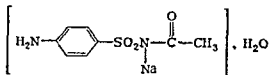
Orally adults are given doses of 0.5—1 g 3—5 times a day for 6—7 days

Total dose for course of treatment 15—25 g Children are given 0.1—0.5 g 3—5 times a day

To be stored in well stoppered glass bottles observing safety precautions (List B)

SULFACYL SOLUBLE Sulfacyl Sodium (Sulfacylum solubile)

Sodium sulfanilacetamide



Synonyms Albucid natrium Sulfacetamidum natrium

White crystalline powder odourless readily soluble in water almost insoluble in alcohol Aqueous solutions are alkaline pH of 10% solution = 8.5

The sodium salt of sulfacyl like sulfacyl itself is an active chemotherapeutic drug which has a marked effect in streptococcal gonococcal pneumococcal staphylococcal and coli bacillary infections

The fact that the drug is readily soluble in water makes possible extensive use for injections solutions are likewise instilled into the conjunctival sac. The toxicity is low and there is no perceptible irritation of the tissues

Can be used for treating infected wounds and infections caused by coli bacilli

Particularly good results are obtained when sulfacyl sodium is used in ocular practice When treating creeping ulcers and other purulent ulcers of the cornea the drug quickly aborts the suppurative process and quickens epithelization of the cornea The drug is also extremely effective in gonorrheal diseases of the eyes of newborn infants and adults Good results are achieved in conjunctivitis and blepharitis

Administered in the form of powders 10 20 and 30% solutions and 10 20 and 30% ointments

Orally sulfacyl sodium can be prescribed in place of sulfacyl adults are prescribed 0.5—1 g 3—5 times a day for 6—7 days Children are prescribed 0.1—0.5 g 3—5 times a day for the same period

Maximal doses for adults single—2 g daily—7 g

Maximal daily dose for children 0.2 g per kg body weight

Wound surfaces are dusted with sulfacyl sodium powder

In ocular practice corneal ulcers are dusted with sulfacyl sodium powder 5—6 times a day until complete epithelization after which instillation of an aqueous solution is begun

Combined treatment is used in gonorrheal diseases of the eye dusting with the powder or instillation of 30% solution along with oral administration.

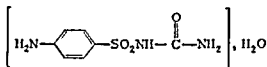
In conjunctivitis and blepharitis the local application of 20—30% ointment is recommended

Available in powder form

To be stored in small well stoppered glass bottles, observing safety precautions (List B)

Rp Sol Sulfacyli solubillis 30% 100
DS Eye drops, 1—2 drops 3 times a day

UROSULFAN (Urosulfanum)
Sulfanilylurea



Synonyms Euvernil Sulfcarbamid Sulfonilcarbamid, Uramid

White or slightly yellowish crystalline powder; odourless, insoluble in water, sparingly soluble in alcohol, insoluble in ether and chloroform, freely soluble in dilute acids and solutions of caustic alkalis

The chemotherapeutic action is most pronounced against staphylococci and coli bacilli. Absorbed rapidly and well from the gastrointestinal tract, a high concentration of the drug is built up in the blood. Mainly excreted by the kidneys. The high concentration in the urine promotes antibacterial action against organisms causing infections of the urinary tract. The drug is only slightly toxic; precipitation in the urinary tract is not observed.

Used in cystitis, pyelitis, cystopyelitis, pyelonephritis, infected hydronephrosis and other infections of the urinary tract. The best effect is achieved in pyelitis and cystitis without disturbance of ureter.

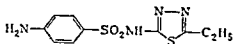
Administered orally in powders and tablets in doses of 0.5—1 g, 3—5 times a day. The average dose for adults is 3 g in 24 hrs. Length of treatment from 6 to 12 or 14 days depending on the peculiarities of the case. Daily dose for children 1—2.5 g (in 4—5 administrations).

Available in powder form and in tablets of 0.5 g.

To be stored in well stoppered bottles, observing safety precautions (List B)

ETHAZOLE (Aethazolum)

2 (p-Aminobenzenesulfonamid) 5 ethyl 3,4-thiadiazole



Synonyms Berlophen, Globucid, Sethadil, Sulphaethylthiadiazole

White or slightly yellowish powder, soluble in dilute acids or alkalis, sparingly soluble in alcohol, insoluble in water and ether. Melting point 180—190°

Has antibacterial activity against streptococci, pneumococci, meningococci, gonococci, coli bacilli, the causative organisms of dysentery and pathogenic anaerobic microorganisms. Only slightly toxic, and tolerated well by patients. Quickly absorbed, excreted for the most part in the urine. Acetylated less than other sulfanilamides and crystals are not formed in the urinary tract, usually causes no changes in the blood.

Used in dysentery, pyelitis, cystitis, pneumonia, erysipelas, angina, peritonitis and wound infections.

Administered orally in the form of powders and tablets. Adults are usually given 1 g every 4 hrs for 6 days in succession, after a 3 day break 1 g is again given every 4 hrs for 3 days. The 1st day of treatment the total dose may be increased to 7 g.

Maximal dose for adults single—2 g daily—7 g

Doses for children up to 2 years old — 0.1—0.3 g every 4 hrs, from 2 to 5 years — 0.3—0.4 g every 4 hrs, from 5 to 12 years — 0.5 g every 4 hrs

In surgical practice ethazole can be used to prevent wound infection up to 5 g of the powdered drug is introduced into the wound cavity, the abdominal cavity, etc. At the same time the drug is administered orally

In infectious ocular diseases, including trachoma ethazole powder or 5% ointment can be introduced into the conjunctival sac

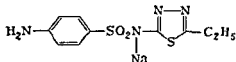
In rare cases, nausea and vomiting may occur when ethazole is taken. If these symptoms do not pass away the dose must be reduced or administration discontinued

Available in powder form and in tablets of 0.5 g

Safety precautions are to be observed in storage (List B)

ETHAZOLE, SOLUBLE; Ethazole sodium (Aethazolum solubile)

Sodium 2 (p aminobenzenesulfonamido) 5 ethyl 3,4 thiazazole



White crystalline powder, freely soluble in water. Aqueous solutions have a pH of 8.5—9.0

possible parenteral administration (intravenously and intramuscularly) as well

The fact that the drug is highly soluble and has no irritating effect makes as administration by mouth

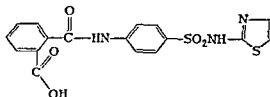
Indications for use are the same as for ethazole. Administered in the form of 10 and 20% solutions at the rate of 0.5, 1 or 2 g of the drug per injection (5—10 ml). Intravenous injections are performed slowly. As soon as the patient's condition permits, parenteral administration of ethazole sodium is discontinued in favour of the oral administration of sulfanilamide drugs

Available in powder form and in ampoules containing 10 ml of 10 or 20% solution

The powder is to be stored in well stoppered bottles in a dry place.

PHTHALAZOL (Phthalazolum)

2 (p Phthalylaminobenzenesulfonamido) thiazole phthalylmorsulfazole



Synonyms Phthalysulfathiazolum; Sulfathalidine, Taleudron, Talidine, Talisulfazol, Thalazol, Thalazone, Thalistatyl

White or slightly yellowish powder, insoluble in water, very sparingly soluble in alcohol, practically insoluble in ether and chloroform, readily soluble in solutions of caustic alkalis and sodium carbonate and bicarbonate

Slowly absorbed from the gastrointestinal tract. When administered orally most of the drug is retained in the intestine. This property of phthalazol along with its activity against intestinal flora makes it highly effective in intestinal infections

Phthalazol is distinguished by its very slight toxicity. It is tolerated well and side effects usually do not occur

Used in dysentery (in acute cases and in exacerbations of chronic cases), ulcerous colitis and gastroenteritis. Also applied to prevent suppurative complications in operations on the intestine.

In acute dysentery, phthalazol is administered orally to adults according to the following schedule

1st and 2nd day 6 g in 24 hrs (1 g every 4 hrs)
3rd . 4th " 4 " " " (1 g every 6 hrs)
5th . 6th " 3 " " " (1 g every 8 hrs)
Total drug for the course of treatment 25—30 g

A second cycle of treatment is given in 5—6 days after the first. 1st and 2nd day—1 g every 4 hrs (every 8 hrs at night) 5 g in 24 hrs, 3rd and 4th day—1 g every 4 hrs (no administration at night), 4 g in 24 hrs, 5th day—1 g every 4 hrs, (no administration at night) 3 g in 24 hrs. Total drug for second cycle 21 g. In mild cases, the total dose for the second cycle of treatment can be reduced to 18 g.

Maximal doses for adults single—2 g, daily—7 g

Children are prescribed smaller doses up to 3 years old—0.2 g per kg body weight daily (given in 3 equal portions during the daytime, without disturbing sleep at night), the drug is given in this dosage for 7 days. Children over 3 years old are given doses of 0.4—0.75 g 4 times a day the size of the dose depending on the age.

In the treatment of other infections, phthalazol is administered to adults in doses of 1—2 g every 4—6 hrs during the first 2—3 days, the next 2—3 days the dose is reduced by half. Children are given a total dose of 0.2 g per kg body weight the first 24 hrs (equal portions every 4 hrs with a break at night). The following days the dose is 0.2—0.3 g every 6—8 hrs.

Treatment with phthalazol can be combined with the administration of levomycetin, biomycin and other antibiotics (see pp 318, 334).

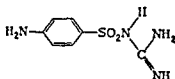
Simultaneously with phthalazol it is an advantage to give sulfanilamide drugs that are absorbed well (sulfadimezine, ethazole, norsulfazol etc.).

Available in powder form and in tablets of 0.5 g

To be stored in well stoppered bottles, observing safety precautions (List B)

SULGIN (Sulginum)

Sulfanilylguanidine, p aminobenzenesulfaguanidine



Synonyms Abiguanil, Aseptilguanidine, Ganidan, Guamid, Guanici, Gusept, Neosulfonamid, Resulfon, Sulfaguanidan, Sulfaguanidinum; Sulphaguanidin

Fine white crystalline powder, sparingly soluble in water and alcohol, almost insoluble in solutions of alkalis, freely soluble in dilute mineral acids. Melting point 189—192°

Sulgin is slowly absorbed. When taken orally, most of the drug is retained in the intestine and is excreted in the feces. It is an effective drug for treating intestinal infections.

Administered orally to adults and children in acute, subacute and chronic bacillary dysentery, acute subacute and chronic colitis, and enterocolitis with diarrhea.

Also used in treating carriers of dysentery and typhoid bacilli and in preparation for operations on the small intestine and colon

In acute intestinal infections adults are given doses of 2 g 6 times a day the 1st day 5 times a day the 2nd and 3rd days 4 times the 4th day and 3 times the 5th day The course of treatment is usually for 5—7 days

In treating dysentery, sulgin is used in the same dosage schedules as phthalazol

Maximal doses for adults single—2 g daily—7 g

Sulgin can be used simultaneously with synthomycin levomycetin biomycin or other antibiotics

Sulgin is slowly absorbed from the intestine and it is therefore an advantage simultaneously to administer drugs which are rapidly absorbed (sulfadime zinc ethazole norsulfazole etc.)

In order to prevent complications after operations on the intestine sulgin is given in a dose of 0.05 g per kg body weight every 8 hrs for 5 days preceding the operation and for 7 days afterwards During treatment diuresis must be maintained in order to avoid side effects involving the urinary tract (precipitation of acetylated sulgin) to this end 2—3 liters of fluid must be ingested daily

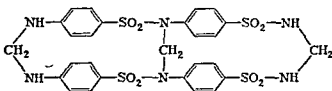
During treatment with sulgin (as well as phthalazol) patients should be given sufficiently large doses of vitamins of the B complex since inhibition of the growth of coli bacilli leads to a decrease in the intestinal synthesis of substances included in the vitamin B complex (thiamine riboflavin nicotinic acid etc.)

Available in powder form and in tablets of 0.5 g

To be stored in well stoppered glass bottles observing safety precautions (List B)

DISULFORMIN (*Disulforminum*)

1, 4 4' N Trimethylene bis (4 sulfanilylsulfanilamide)



Fine white crystalline powder insoluble in water and dilute mineral acids freely soluble in solutions of caustic alkalis and carbonates Melting point 190—200°

Disulformin is similar in action to the sulfanilamide drugs especially phthalazol and sulgin It is slowly absorbed and is therefore chiefly effective in infectious diseases of the intestine

In the alkaline medium of the intestine disulformin is hydrolyzed with the liberation of formaldehyde which may play a certain role in the therapeutic effect

Used in the treatment of acute and chronic enterocolitis and acute dysentery

Administered orally Adults are given 1 g 6 times a day for 4—5 days (every 3 hrs with a break at night) Children up to 3 years old are given 0.1—0.2 g per kg body weight daily (4—6 administrations) Children over 3 years old are given doses of 0.5—0.75 g 4—6 times a day

If treatment is not sufficiently effective another 3—4 days of treatment is given with the doses specified after a break of 5—7 days During treatment patients should not eat food rich in protein since this lowers the activity of the drug Disulformin is not used in treating carriers of dysentery bacilli since the drug has no disinfecting action

Available in powder form and in tablets of 0.5 and 1 g

To be kept in well stoppered bottles in a cool place

C Antituberculosis drugs

a) Isonicotinic acid hydrazide and its derivatives

ISONIAZID (Isoniazidum)

Hydrazide of isonicotinic acid hydrazide of 4 pyridinecarboxylic acid



Synonyms Andrazide Armazide Chemiazid Cotiazine Dibutin Difori Dinacrin Ditubin Ertuban Eulizon Hidrazinil Idrasil INH Isonin Isocot Isolyn Isonicid Isonico Isonizid Isotebecid Lanlazid Mybazan Neoleben Niadrin Nicazid Niconyl Nicotiline Nicozide Nidaton Nydrazid Pelazi Pycazide Pyreazid Pyrizidin Rimison Tebaxin Tebaconin Tibinide Tibizi Tibusan Tizin Tubazid Tubeco Tyvid Vadrazine Zinadon Zonazide

White crystalline powder bitter taste soluble in water sparingly soluble in alcohol Melting point 170—171°

Isoniazid was the first derivative of isonicotinic acid to be used as an antituberculosis agent Other drugs of this series (phthivazid saluzid metazid larisan etc) can be considered derivatives of isonicotinic acid hydrazide

Isoniazid has high bacteriostatic activity against *Mycobacterium tuberculosis* It has no marked chemotherapeutic action against other widely distributed pathogenic organisms

Isoniazid is absorbed well from the gastrointestinal tract The maximal concentration in the blood is found 1—3 hrs after administration by mouth a bacteriostatic concentration is maintained in the blood for 6—24 hrs after taking a single dose The drug readily penetrates through the hematoencephalic barrier and can be detected in the different body tissues and fluids Excreted for the most part by the kidneys

When injected intramuscularly isoniazid is excreted more rapidly and the concentration in the blood is substantially no higher than that created by like doses administered by mouth

Isoniazid is used for the treatment of all forms of pulmonary tuberculosis in adults and children It is most effective in the following cases early and acute forms of the tuberculous process the initial phase of the primary complex infiltrative bronchadenitis infiltrative pneumonic pulmonary tuberculosis and particularly acute miliary and subacute hematogenous disseminated pulmonary tuberculosis as well as chronic fibrocavernous pulmonary tuberculosis in a period of exacerbation and when there are symptoms of toxemia It is also used in tuberculosis of the larynx and oral cavity tuberculosis of the mucous membrane of the gastrointestinal tract tuberculosis of the serous membranes tuberculosis of the bones and joints and lupus

In old cirrhotic forms of tuberculosis isoniazid has no marked therapeutic effect

In tuberculous meningitis miliary tuberculosis and tuberculosis of the kidneys isoniazid is prescribed in combination with streptomycin and sodium paraaminosalicylate

In cases of mixed infection other antibacterial drugs must be given simultaneously with isoniazid antibiotics and sulfonamides

Isoniazid is usually administered orally but when necessary it can be administered in the form of rectal suppositories or intramuscularly Intramuscular injections are somewhat painful The drug can also be used in the form of aqueous solutions for irrigating fistulas and cavities

Therapeutic doses of isoniazid range from 3 to 5 mg per kg body weight daily (in 2-3 administrations). Usually 0.1-0.2 g per day is given the first 2 or 3 days and then if the drug is tolerated well the dose is increased to 0.3-0.4 g per day. When administered rectally and intramuscularly the same doses are prescribed. 1 and 2% aqueous solutions are used for irrigating cavities. The single dose for instillation into a cavity is 0.05-0.2 g.

The length of treatment is individualized depending on the course of the disease, the effectiveness of the drug and the extent to which it is tolerated. The average course of treatment is for 3-4 months in tuberculous meningitis and military tuberculosis treatment is continued for up to a year or more.

The toxicity of isoniazid is relatively high. During treatment such side effects as vertigo, headache, irritability, euphoria, insomnia, tremor and convulsive twitching of lower extremities, general convulsions, syncope and other disturbances of the function of the central and peripheral nervous systems may occur, as well as disturbance of the functions of the organs of the gastrointestinal tract, nausea, vomiting, constipation and deterioration of appetite. At times there are allergic skin reactions, icterus, palpitation, substernal pain, flushing of the face, lowering of the temperature and retarding of blood coagulation.

As a rule these symptoms soon pass away when the drug is withdrawn.

Polynuritis is among the most serious complications; it may persist after administration of the drug has been discontinued. In epileptic patients attacks may become more frequent.

If complications set in the dose must be reduced and if necessary administration of the drug must be stopped.

In order to prevent complications involving the nervous system it is advisable to prescribe vitamins B₁ and B₆ (pyridoxine). It has been reported that the administration of glutamic acid diminishes symptoms involving the cardiovascular and central nervous systems.

Contraindications to the use of isoniazid: epilepsy, tendency to convulsions, mental diseases, syphilis of the nervous system, past history of poliomyelitis, functional insufficiency of kidneys and liver, pronounced atherosclerosis.

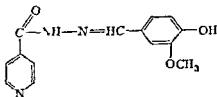
When carrying out treatment with isoniazid the possibility of the development of drug tolerance in the tuberculosis bacilli must be taken into account. Resistant forms may appear during the first months of treatment. The possibility of resistant forms appearing is lessened when isoniazid is used in combination with PAS and streptomycin.

Available in powder form and in tablets of 0.1 g.

To be stored in tightly closed containers observing safety precautions (List B).

PHTHIVAZID (Phthivazidum)

Isonicotinoyl (3-methoxy-4-hydroxybenzal) hydrazone



Pale yellow or yellow, fine crystalline powder, faint odour of vanillin, tasteless, almost insoluble in water, sparingly soluble in alcohol, freely soluble in inorganic acids and alkalis.

Similar to isoniazid in chemotherapeutic properties but less toxic.

Phthivazid is absorbed well from the gastrointestinal tract and easily penetrates into the different body tissues and fluids. It is used in all forms of pulmonary tuberculosis in adults and children, both in fresh cases of the disease.

and in a period of exacerbation of chronic processes when there are symptoms of toxemia. It is also indicated in tuberculosis of the larynx and oral cavity, tuberculosis of the serous membranes, tuberculosis of the peripheral lymph nodes, tuberculosis of the bones and joints, tuberculosis of the skin, etc.

In *miliary tuberculosis* and *tuberculous meningitis*, phthivazid is used in combination with streptomycin and PAS. When phthivazid is used in combination with streptomycin for the treatment of *tuberculous meningitis*, phthivazid is given orally while streptomycin is administered intramuscularly or subarachnoidally.

Like isoniazid, phthivazid is not a substitute for collapse therapy and other surgical methods of treating tuberculosis. If warranted by the indications, it can be used along with those methods.

In cases of mixed infection, other antibacterial drugs must be given simultaneously with phthivazid.

Phthivazid is administered orally before meals in the form of powders or tablets. The single dose for adults is 0.3–0.5 g administered 3–4 times a day; the optimal daily dose is 1.2–1.5 g. Single doses for children up to 2 years old — 0.1–0.2 g (0.3–0.5 g daily); from 3 to 7 years — 0.2–0.3 g (0.6–0.7 g daily); from 8 to 12 years — 0.3–0.5 g (0.9–1 g daily).

In *tuberculous meningitis*, the dose is increased: adults are given 1.5–2 g daily (0.5 g 3–4 times a day); juveniles — 1–1.5 g daily; children — correspondingly less.

When phthivazid is not tolerated well (nausea, vomiting) or when there is difficulty in swallowing, it can be administered rectally in suppositories; the dose being increased 50 or 100%.

It has been reported that phthivazid is effective in pulmonary tuberculosis when used in the form of an aerosol (0.2–0.5 g per inhalation twice a day).

Phthivazid is often given in combination with PAS or streptomycin. Such treatment is usually more effective and there is less possibility of resistant forms of tuberculosis bacilli developing in the patient's body.

Phthivazid can be used in hospitals and sanatoria and on an out-patient basis. The length of treatment is individualized depending on the peculiarities of the disease, the effectiveness of treatment and so on. The course of treatment may continue from 2½–3 months to a year or more.

In *lupus*, phthivazid is prescribed in a dose of 0.2–0.3 g 3–4 times a day. Total drug for the course — 40–60 g. In order to achieve a clinical cure, such courses of treatment are repeated 2–3 times with breaks of 1 month between.

It has been reported that phthivazid is effective in *actinomycosis* of the internal organs. The drug is prescribed in the same doses as in the treatment of pulmonary tuberculosis. Penicillin is administered simultaneously and the necessary surgical intervention carried out.

Phthivazid is usually tolerated well but side effects sometimes occur: vertigo, headache, pain in the region of the heart, dermatitis, paresthesia, dysuric symptoms, nausea, vomiting and loss of appetite. In such cases the dose must be reduced or the drug temporarily withdrawn.

Maximal doses for adults: single — 1 g daily — 2 g.

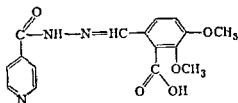
Maximal doses for children: up to 6 months old — single — 0.1 g daily — 0.3 g; from 6 months to 1 year — single — 0.15 g daily — 0.45 g; 2 years — single — 0.2 g daily — 0.5 g; 3–4 years — single — 0.3 g daily — 0.6 g; 5–6 years — single — 0.35 g daily — 0.7 g; 7–9 years — single — 0.4 g daily — 0.8 g; 10–14 years — single — 0.5 g daily — 1 g.

Contraindications: stenocardia and decompensated heart disease, organic diseases of the central nervous system, non-tuberculous diseases of the kidneys with impairment of the excretory function.

Available in powder form and tablets of 0.1, 0.3 and 0.5 g.

SALUZID (Saluzidum).

Isonicotinoyl (2 carboxy 3,4 dimethoxybenzal) hydrazone



Yellow green fine crystalline powder, sparingly soluble in water, insoluble in ether, readily soluble in alkalis and inorganic acids Melting point 196—203°

In chemotherapeutic properties does not differ substantially from phthivazid

Absorbed well from the gastrointestinal tract and quickly penetrates into the body fluids and tissues

Indications and contraindications are the same as for phthivazid

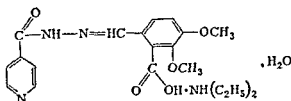
Administered orally in a dose of 0.5 g 2—3 times a day

Available in powder form and in tablets of 0.5 g

To be stored in a dry place protected from light, observing safety precautions (List B)

SALUZID, SOLUBLE (Saluzidum, soluble)

Diethylammonium salt of isonicotinoyl (2 carboxy 3,4 dimethoxybenzal) hydrazone



White or slightly yellowish crystalline powder, readily soluble in water and alcohol, insoluble in ether

Soluble saluzid is used for achieving a general and local effect in the following forms of the tuberculous process tuberculosis of the meninges, pleura, serous membranes and mucous membranes of the upper respiratory passages, tuberculosis of the genitourinary system, tuberculosis of the lymph nodes fistular forms of tuberculosis of diverse localization, tuberculosis of the skin, tuberculous affections of the eye Soluble saluzid is absolutely indicated in cases of tuberculous meningitis when streptomycin is not tolerated by the patient or when the pathogenic organism is resistant to the antibiotic.

Soluble saluzid can be administered subcutaneously, intramuscularly, intravenously or subarachnoidally, it can also be used locally for instillation into cavities and for irrigation

The single dose for subcutaneous and intramuscular injections is 10 ml 5 or 10% solution (0.5—1 g of the drug), the daily dose may come to 2 g

Not more than 10 ml 5% solution is administered intravenously, the injection is made slowly — 1 ml per min

5% solution is used for subarachnoidal injections

5 and 10% solutions are used for instillation into cavities The drug may be diluted to the desired concentration with sterile isotonic saline

In tuberculosis of the upper respiratory passages the drug may be administered intratracheally with a laryngeal syringe in a dose of 2—3 ml 5% solution. Total number of administrations for the course from 10 to 20 or 30.

Soluble saluzid can be used in the form of an aerosol for treating various forms of pulmonary tuberculosis. 2.5—3 ml of 10% solution are used for an inhalation. Adults are given 2—3 inhalations per day, and children 2.

The course of treatment is for 20—60 days or more.

In tuberculosis of the genitals in females a 5 or 10% solution of saluzid is administered intramuscularly and regionally (cervix or vaginal vaults), 5—10 ml per day. 100—250 ml of solution is used for the course.

It is advisable to combine administration of soluble saluzid with the administration of phthivazid, streptomycin and PAS.

In tuberculous meningitis, soluble saluzid can be injected into the spinal canal. 1.5—2 ml 5% solution per kg body weight (patients weighing 60 kg are given 1.8—2.4 ml 5% solution or 90—120 mg of the drug). If there is good tolerance the dose per injection can be increased to 2.5 mg per kg body weight. Punctures are made every day or each second day depending on the phase of the disease and the patient's condition. The solution is injected endolumbarly. If there are special indications (blocking of subarachnoid space) the drug may be administered suboccipitally. As in treatment with streptomycin the number of punctures is determined by the patient's clinical condition and sanitation of the spinal fluid.

Endolumbar administration should be combined with intramuscular injections of streptomycin or soluble saluzid and oral administration of phthivazid, saluzid or PAS in the usual dosage.

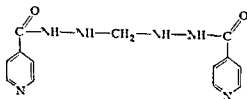
Available in powder form and in ampoules containing 1, 2 and 10 ml 5% solution or 10 ml 10% solution.

To be stored in sealed ampoules in a place protected from light.

Ampoules should be opened immediately before use. Solutions should not be kept in open containers because of the possibility of a precipitate forming.

METAZID (Metazidum)

1. 1 Methylene bis isonicotinoylhydrazine



White crystalline powder, bitter taste, soluble in mineral and organic acids, insoluble in water and the usual organic solvents. Melting point 175—180°.

Similar to phthivazid in antituberculosis activity. Considerably less toxic than isoniazid. Absorbed well from gastrointestinal tract and penetrates into spinal fluid. The bacteriostatic activity of the spinal fluid is higher than when like doses of phthivazid are taken.

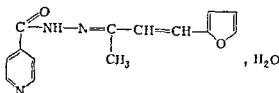
Indications are the same as for phthivazid.

Administered orally before meals in the form of powders or tablets. Adults are given 0.2 g twice a day the first few days if tolerated well, the dose is increased to 0.3—0.5 g 3 times a day. Children are given 0.02 g per kg body weight daily, this dose being divided for 2—3 administrations. Length of treatment is the same as for phthivazid.

Metazid is usually tolerated well but when used for long periods the same complications may occur as when other derivatives of isonicotinic acid hydrazide are taken.

To be stored in a dry place observing safety precautions. (List B)

LARUSAN (Larusanum)
Isonicotinoylhydrazide furfuralacetone



Light yellow powder odourless and tasteless sparingly soluble in water soluble in organic solvents and mineral acids Darkens under the influence of direct sunlight Melting point 190—191°

Similar to phthivazid in antibacterial action against tuberculosis bacilli and in indications contraindications and possible complications

Administered orally adults being given 0.1—0.3 g 3 times a day The therapeutic effect is usually manifested sufficiently well when the daily dose comes to 0.6 g Children from 5 to 8 years old are given 0.05 g 3 times a day older children — 0.1 g 3 times a day

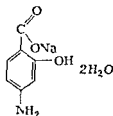
Length of treatment is the same as for phthivazid

To be stored in well stoppered bottles in a place protected from light observing safety precautions (List B)

b) Derivatives of Para Amino Salicylic Acid

SODIUM PARA AMINOSALICYLATE PAS (Natrium para aminosalicylatum) (Natrii para aminosalicylas)

Sodium 4 amino 2 hydroxybenzoate



Synonyms Aminacyl Aminopar Aminosalyl Aminox Apacil Bactylan Eupasal Pamisyl Para Pas Paramisan Parasal Pasalicylum solubile Pro pasa Tebaminol Teebacin Tubopas Wofapas

White yellowish or pinkish fine crystalline powder freely soluble in water sparingly soluble in alcohol Solutions are sterilized by holding at 100° for 30 min

PAS has marked bacteriostatic activity against *Mycobacterium tuberculosis* Absorbed well from gastrointestinal tract Used in the treatment of various forms of tuberculosis especially effective in infiltrative processes and exacerbations of chronic pulmonary fibroso cavernous tuberculosis often given in combination with phthivazid streptomycin and other antituberculosis drugs

Administered orally in the form of powders granules or dragees at the rate of 0.2 g per kg body weight daily Adults are usually given doses of 2—3 g 30—60 min after meals 4 times a day Single doses for children range from 0.25—0.5 g to 2 g The drug is drunk down with alkaline mineral water a 2% solution of sodium bicarbonate or milk

For emaciated adult patients of small weight and for those with poor tolerance for the drug the daily dose should be reduced to 6—8 g For patients who tolerate the drug well but in whom there is no marked effect in 2—3 weeks when

the usual doses are taken the daily dose may be increased to 14–16 g (single doses of 3.5–4 g). In effective cases treatment of patients with pulmonary tuberculosis continues roughly up to 3 months or more.

In tuberculous empyema, 20–30 ml of 5–10% aqueous solution of PAS is instilled into the pleural cavity but only after the excavation of the exudate and lavage of the pleura.

The intravenous administration of the sodium salt of PAS (up to 500 ml 3–4% solution by the drip method over a period of 5 hrs) has recently been proposed in cases requiring the rapid building up of a high concentration of the drug in the blood and tissues (tuberculous meningitis, miliary tuberculosis, etc.), and when the tuberculosis bacilli are resistant to streptomycin and derivatives of isonicotinic acid hydrazide. To prevent possible thrombosis of the veins it is advisable to give patients heparin.

In the treatment of tuberculosis of the skin PAS is administered orally. Adults are given 10–12 g daily, and children from 2 to 8 g, depending on the age. The total dose for the course of treatment comes to 600–1000 g.

Side effects may occur when PAS is used: coryza, conjunctivitis, urticaria, eruptions on the mucous membrane of the mouth, chills, dyspnea, meteorism, nausea and at times vomiting, affections of the liver and kidneys are possible, as well as leukopenia and anemia. If side effects develop the dose should be reduced. In cases of intolerance, treatment must be discontinued. Treatment should be carried out under the careful observation of a physician; regular examinations of the urine and blood are necessary and the functional condition of the liver must be checked.

When there is up to 1% albumin in the urine the use of the drug is still possible. If the concentration of albumin rises and other symptoms of irritation of the kidneys appear the dose of PAS must be reduced or treatment discontinued.

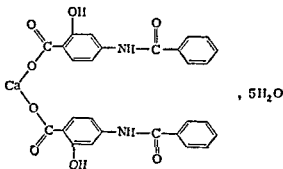
In large doses PAS has an antithyroid action; when used for lengthy periods there may be a strumogenic effect (see p 279). This property of PAS must be borne in mind if there is hypofunction of the thyroid in tuberculosis patients. At the same time the drug may be beneficial in tuberculosis patients suffering from hyperthyroidism.

Available in powder form and in tablets of 1 g.

To be stored in well stoppered bottles in a dry place protected from light.

BEPASC (Bepascum)

Calcium *p*-aminobenzoylamino-salicylate



White powder. Insoluble in water.

Bepasc has a chemotherapeutic action in tuberculosis similar to para amino salicylic acid of which it is a derivative. In the body the acid is slowly liberated; it is the free acid which has a therapeutic effect. A more constant concentration of PAS in the blood is achieved when bepasc is used.

Bepasc is administered orally, indications for use being the same as for PAS. The daily dose is 12–16 g in 4–5 administrations. The drug can be used in combination with phthivazid and streptomycin.

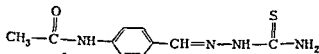
Bepasc is tolerated well but dyspeptic symptoms are sometimes observed, as well as allergic reactions (skin eruptions, pruritus), vertigo and pain in the region of the heart. If there should be pronounced side effects the dose is temporarily reduced or treatment discontinued.

Treatment should be carried out under the careful observation of a physician (see PAS).

c) Thiosemicarbazones

TIBON (Tibonium).

p-Acetaminobenzaldehyde thiosemicarbazone



Synonyms: Ambathizonum, Amithiozon, Benzothiozone, Conteben, Dizan, Myvizon, Neotibil, Neustab, Parazone, Tebethion, Teebazone, Thiacefazonium, Thiomicid, Thioparamizone, Tibion, Tibisan, Tazone, Tubercazon, Vitazone.

Light yellow, fine crystalline powder, bitter taste, almost insoluble in water, sparingly soluble in alcohol.

Tibon has marked bacteriostatic activity against tuberculosis bacilli, but is used to only a limited extent because of its relatively high toxicity, usually administered in combination with phthivazid, PAS, streptomycin and other anti-tuberculosis drugs to heighten the therapeutic effect (as a representative of a different class of chemical compounds) and lessen the possibility of the appearance of resistant forms of *Mycobacterium tuberculosis*.

Chiefly used in tuberculosis of the mucous and serous membranes, lymphadenitis, scrofuloderma and specific fistulas, less effective in pulmonary tuberculosis. Not used in tuberculous meningitis. In some cases has a favourable effect in leprosy, especially in early stages of the disease.

Administered orally in the form of powders, tablets or dragees. In the treatment of tuberculosis, usually prescribed according to the following schedule: 1st week — 0.01–0.015 g 2–3 times a day, 2nd week — 0.025 g twice a day, 3rd week — 0.05 g twice a day, 4th week — 0.05 g 3 times a day or 0.1 g twice a day.

Taken after meals, drunk down with a glass of water, tea or milk.

Maximal doses for adults: single — 0.1 g, daily — 0.2 g.

In leprosy the single dose is 0.025–0.1 g, daily dose — 0.1–0.2 g. Administered in cycles of 10 days treatment followed by a 4 day break. After 12–14 cycles a break of 1–1½ months is made, after which the course of treatment is repeated. Treatment is lengthy and is carried out in combination with general tonics, physiotherapeutic methods, etc.

A 1% sterile suspension of tibon in oil, glycerol or isotonic saline is sometimes used in the treatment of tuberculous empyema, 30 ml of the suspension is instilled into the pleural cavity once or twice a week after removal of the purulent exudate and lavage of the cavity with isotonic saline or 1–2% PAS solution.

Complications may occur when tibon is used: headache, nausea, dermatitis and deterioration of appetite. In rare cases albuminuria and hepatitis may develop, and at times agranulocytosis.

If side effects should develop, the dose is reduced, if small doses (0.01–0.025 g) are not tolerated, treatment with tibon should be discontinued.

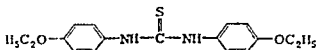
Available in powder form and in tablets of 0.025 and 0.05 g.

To be stored in a place protected from light, observing safety precautions (List B).

d) Derivatives of thiocarbamide

ETHOXYD (Aethoxydum)

4:4 Diethoxythiocarbamide



White crystalline powder insoluble in water. Melting point 167—169°

Ethoxyd has high bacteriostatic activity in respect to the causative organism of tuberculosis, does not act on other bacteria.

Used in the treatment of various forms of tuberculosis administered in combination with phthivazid and streptomycin to prevent the development of resistant forms of tuberculosis bacilli and also in the presence of resistant forms or when other antituberculosis drugs are not tolerated.

Ethoxyd is taken orally before meals. The dose for adults during the first few days of treatment is 0.2—0.25 g daily; the dose is then gradually raised over a period of 1 week to 0.5 g twice a day. Children are given smaller doses according to their age. The drug is used for a lengthy period — up to 6 months or more.

Ethoxyd is usually tolerated well but in isolated cases there may be allergic skin reactions (pruritus, urticaria, etc.), headache and elevated temperature. If there should be marked side effects the dose is lowered or treatment temporarily discontinued.

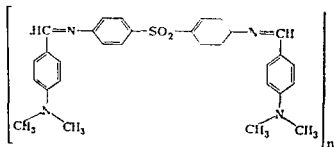
Available in powder form and in tablets of 0.25 and 0.5 g.

To be stored under ordinary conditions observing safety precautions (List B).

e) Miscellaneous compounds

SULFONIN (Sulfoninum)

Polymer obtained by condensing 1:4 diaminodiphenylsulfone with *p*-dimethylaminobenzaldehyde.



Synonym: Sulfamethin

Yellow powder, faint characteristic odour, tasteless, sparingly soluble in water, alcohol and organic solvents.

Used in the treatment of tuberculosis of the bones and joints, periarticular tuberculous lesions situated at the surface in joints of the extremities, tuberculous lesions in the flat bones and small long bones, fistulas (mainly those with short canals), etc.

Administered in the form of a 5% suspension in glycerol or a 10% ointment.

The sterile suspension is introduced into lesions after warming and thorough shaking. The suspension is injected into periarticular and bone foci with

a thick needle after anesthesia of the tissues with a 0.5% solution of procaine hydrochloride 1—2 ml of the suspension being applied once in 7—10 days. In cases of accumulating abscesses, 1—3 ml of the suspension is instilled after evacuation of the pus, usually once a week. In cases of fistulas, 1—2 ml is instilled once or twice after toilet of the skin. A 10% ointment is also used in fistulas and ulcers. In severe destructive affections of the joints streptomycin is administered intramuscularly simultaneously with application of sulfonin.

In isolated cases side effects may occur when sulfonin is used: elevated temperature, general malaise and intensified pain at the focus of affection. These symptoms usually pass away of themselves in 1—2 days. During treatment an examination of the blood and urine must be made at least once in 2 weeks.

To be stored in a cool, dry place, protected from light, observing safety precautions (List B).

JUGLONE (*Juglonum*)

5-Hydroxy 1, 4-naphthoquinone



Yellow-orange crystalline powder sparingly soluble in water, soluble in alcohol and ether. Melting point 154—155°.

Proposed for the treatment of tuberculosis of the skin (M. V. Borzov, L. N. Aizenberg and A. G. Mezhevalova).

Applied locally in the form of ointments and aqueous alcoholic oil and ether solutions. Strong concentrations cause necrosis and sloughing of the surface tissues, weak concentrations promote subsequent epithelization. Treatment is begun with destructive concentrations (1, 2 or 4%) and then as the course of the pathological process changes, a shift is made to weaker concentrations (0.25 or 0.5%).

Juglone ointment is used in the treatment of lupus vulgaris, scrofuloderma and tuberculous warts. A dressing with the ointment is applied to the lesions once or twice a day for 3 days in succession. The dry brownish-black scab which forms in 3—4 days is removed with oil, petrolatum or an indifferent ointment.

After removal of the scab, ointments with a large and with a small content of juglone are applied alternately until the formation of a cicatrix.

A 1:5000 aqueous alcoholic solution of juglone is used as a lotion and for compresses in the treatment of patients with scrofuloderma. Wet dressings and compresses are applied to the ulcerated areas or to the unopened scrofulous gummas. A 1:10,000 solution is used for gargling in lupus of the mucous membrane of the oral cavity.

In order to accelerate epithelization, lesions are swabbed with a solution of juglone in ether (1, 2 or 4%). Such a solution can also be used for the treatment of chronic eczema, trichophytosis of the smooth skin and chronic epidermophytosis.

Juglone ointments are prepared with petrolatum or lanolin, the maximum solubility in petrolatum is 4%. In order to abate the pain, ethyl aminobenzoate is added to the ointment to give a concentration of 5—10%, depending on the concentration of juglone.

When preparing aqueous alcoholic solutions 0.2 g of juglone is ground to a fine powder and dissolved in 50 ml 96° ethanol, this is the stock solution. A 1:5000 solution is made by adding 5 ml of the stock solution to 95 ml of distilled water, and thoroughly shaking. A 1:10,000 solution is made by adding 5 ml of the stock solution and 5 ml of alcohol to 190 ml of distilled water.

Aqueous alcoholic solutions can be kept for 5 days

In order to make an aqueous alcoholic suspension (1:1000 or 1:2000) 1 g juglone is thoroughly pulverized and 20 ml 96° ethanol added followed by 1000 or 2000 ml distilled water

Juglone ointment causes a burning sensation when applied lasting from several minutes to 2 hrs. Solutions and suspensions ordinarily cause no burning action

When the process is disseminated juglone is administered in stages being led successively to separate areas

To be stored in stoppered bottles in a place protected from light, observing the precautions (List B)

CALCIUM AUROTHIOPROPANOL-SULFONATE

An oil suspension of the gold preparation calcium aurothiopropanol sulfonate $[(CH_3)_2SAu-CH(OH)-CH_2-SO_3]_2Ca$ and calcium gluconate

Synonyms Chrysanol Oleochrysin

Available in ampoules containing 2 ml 5 and 10% suspension 1 ml of 5% suspension contains 0.015–0.0185 g gold 1 ml 10% suspension contains 0.03–0.07 g gold

Chiefly used in lupus erythematosus and also in the treatment of infectious arthritis. Until the appearance of streptomycin, PAS, phthivazid and other modern chemotherapeutic drugs it was used relatively widely for the treatment of fresh forms of tuberculosis of the lungs and larynx

Administered intramuscularly before making injections the suspension is mixed and thoroughly shaken. Doses are individualized depending on the character and course of the disease and the extent to which the drug is tolerated

Initial dose is usually 2 ml of 5% suspension. 10 injections are given at intervals of 2–5 days. 10 injections each of 2 ml 10% suspension are then given at the same intervals. A total of 20–25 injections are given

During treatment watch must be kept on the condition of the skin and mucous membranes and also on the blood and urine. On the appearance of dermatitis, rheumatism, pathological changes in the blood picture or albumin and blood in the urine the intervals between injections must be lengthened or administration of drug discontinued

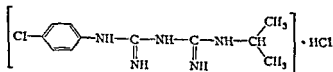
Contraindications: miliary tuberculosis and tuberculous meningitis, caseous pneumonia, old fibroscavertous forms and cirrhotic processes, as well as diseases of the kidneys of non tuberculous character, decompensated heart disease, diabetes, cachexia and other serious diseases

D Drugs for the treatment of protozoan infections

a) Antimalarial drugs

CHLORGUANIDE HYDROCHLORIDE (Chlorguanidum hydrochloricum)

N_1 p Chlorophenyl N_3 isopropylbiguanide hydrochloride



Synonyms: Balasol, Bigumal, Chloriguane, Diguanil, Drinupal, Guanatol, Ludrine, Palusil, Plasim, Proguanide, Proguanil, hydrochloridum, Proguanil, Trian

White crystalline powder, odourless, bitter taste, sparingly soluble in alcohol, sparingly soluble in water (1% at 20°)

Chlorguanide like quinacrine is a therapeutic and prophylactic antimalarial, which acts chiefly on the asexual forms of the etiologic agent of malaria — the schizonts — but it is considerably more effective than quinacrine in the treatment of

atment of tropical malaria A single course of systematic treatment with chlorguanide leads to a radical cure of this form of malaria in 95—98% of the cases Under the influence of chlorguanide the gametocytes of *Plasmodium falciparum* are injured, they either completely lose the ability of developing within the mosquito, or if development does begin it is abortive and does not lead to the formation of sporozoites ("gamostatic action")

Chlorguanide hydrochloride is quickly absorbed from the gastrointestinal tract, it is excreted more rapidly than quinacrine, for the most part by the kidneys

When carrying out a systematic course of treatment chlorguanide is administered for 5 days according to the following schedule

Day of treatment	Daily dose, g	Manner of administration
1st	0.6	0.3 g twice a day
2nd-5th	0.3	0.3 g once a day

In severe forms of tropical malaria treatment is continued for 7 days

Chlorguanide is also used in combination with methoxy diethylaminopropyl amino quinoline being administered for 5 days according to the following schedule

Day of treatment	Daily dose for adults, g		Manner of administration
	Chlorguanide	Methoxy diethyl aminopropylamino quinoline	
1st	0.6	0.06	In 2 doses
2nd-5th	0.3	0.06	In 1—2 doses

Systematic treatment with compound tablets containing quinacrine, chlorguanide and methoxy diethylaminopropylamino quinoline is carried out for 7 days, 3 tablets being given daily (a total of 0.3 g quinacrine 0.3 g chlorguanide and 0.06 g methoxy diethylaminopropylamino quinoline), to be taken in one or two doses

Maximal doses of chlorguanide hydrochloride for adults single — 0.3 g daily — 0.6 g

When chlorguanide hydrochloride is given to children the dose is reduced according to the age

Age	Daily dose, g
Up to 1 year	0.025
1—2 years	0.05
2—4 years	0.075
4—6 "	0.1
6—8 "	0.15
8—12 "	0.15—0.2
12—16 "	0.25
over 16 years	0.3

Compound tablets containing methoxy diethylaminopropylamino quinoline (grey tablets and brownish yellow tablets) are not prescribed for infants up to 1 year old

Maximal doses of chlorguanide hydrochloride for children up to 6 months old single—0.0125 g daily—0.025 g from 6 months to 1 year single—0.0125 daily—0.025 g 2 years single—0.025 g daily—0.05 g 3—4 years single—0.03—0.01 g daily—0.06—0.08 g 5—6 years, single—0.04—0.05 g daily—0.08—0.1 g 7—9 years single—0.75 g, daily—0.15 g, 10—11 years single—0.1—0.125 g daily—0.2—0.25 g

Spring treatment for the prevention of relapses is carried out according to the same dosage schedules as the systematic treatment. For public and individual chemo prophylaxis 2 tablets of chlorguanide hydrochloride and methoxy diethyl aminopropylamino quinoline are prescribed twice a week (e.g., on the 1st and 4th day of the week) during the entire epidemic season.

Malarial coma is treated with chlorguanide in the following way: at the first symptoms indicating the possibility of the patient developing coma the daily dose of chlorguanide is increased to 0.8 g which is given orally at intervals of 6 hrs. 2 doses of 0.3 g and 1 dose of 0.2 g. If it is impossible to give the drug orally because the patient is unconscious it is injected intravenously in the form of a 1% solution. The single dose should not exceed 0.15 g (15 ml 1% solution) it is injected slowly over a period of 5 min. The administration can be repeated in the same dose in 1—6 hrs. The daily dose intravenously should not exceed 0.4 g. When the patient regains consciousness chlorguanide hydrochloride is administered orally in a daily dose of 0.3 g. The course of treatment should be continued 7 days. 1% chlorguanide hydrochloride solutions for injections is prepared with 0.5—0.6% sodium chloride solution. Sterilized by holding at 100° for 30 min.

Chlorguanide is usually tolerated well by patients (including pregnant women and children). At times there is a transitory increase in the number of leukocytes in the peripheral blood young forms of neutrophils appear, and a small number of erythrocytes are observed in the urine.

When chlorguanide or pyrimethamine is used for lengthy periods in insufficient doses resistance to the drug develops fairly easily in the malarial parasites.

Chlorguanide hydrochloride is available in the following forms: a) white tablets containing 0.1 g chlorguanide (for adults) or 0.5 g chlorguanide (for children); b) grey tablets containing 0.1 g chlorguanide and 0.02 g methoxy diethylaminopropylamino quinoline (for adults) or 0.05 g chlorguanide and 0.01 g methoxy diethylaminopropylamino quinoline (for children); c) brownish yellow tablets containing 0.1 g quinacrine 0.1 g chlorguanide and 0.02 g methoxy diethylaminopropylamino quinoline (for adults) or 0.05 g quinacrine 0.05 g chlorguanide and 0.01 g methoxy diethylaminopropylamino quinoline (for children); d) chlorguanide hydrochloride powder for the preparation of 1% solution for intravenous injections (to be given only in the comatose form of malaria).

To be stored in a dry place protected from light observing safety precautions (List B).

Rp Chlorguanide hydrochloride 0.1

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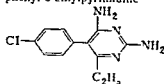
S 3 tablets to be taken twice the 1st day

3 tablets to be taken once a day the remaining

4 days (for adults)

PYRIMETHAMINE (Pyrimethaminum)

2,4-Diamino-5-p-chlorophenyl-6-ethylpyrimidine



Synonyms Chloridin, Daraprim Malocide

White crystalline powder, odourless and tasteless, insoluble in water, soluble in alcohol Melting point 237—238°

Pyrimethamine is similar to chlorguanide in the character of its action but is considerably more potent and at the same time less toxic Taken orally

In the treatment of acute attacks of malaria adults are prescribed 0.025—0.05 g daily, in 1—2 doses, over a period of 2—4 days, total dose for the course—0.1—0.2 g Children are prescribed the following daily doses up to 5 years old—0.005 g, from 6 to 11 years—0.01 g, from 12 to 15 years—0.02 g, 16 years and older—0.025 g To be given for 3 days

After the course of treatment of 3 day malaria an additional course of treatment is given to prevent a relapse For public and individual chemo prophylaxis, pyrimethamine is prescribed once a week during the entire epidemic period Adults are given doses of 0.025 g, children—0.005—0.01 g

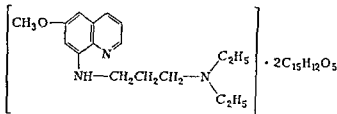
Pyrimethamine is usually tolerated well but its prescription is not advisable in diseases of the hemopoietic organs and kidneys

Available in powder form and in tablets of 0.025 g

To be stored in a place protected from light, observing safety precautions (List B)

METHOXY-DIETHYLAMINOPROPYLAMINO QUINOLINE

6 Methoxy 8 (3' diethylaminopropyl) aminoquinoline methylene bis salicylate



Synonym Plasmocid

Yellow orange powder faintly bitter taste insoluble in water sparingly soluble in alcohol insoluble in other organic solvents

Methoxy diethylaminopropylamino quinoline is a synthetic antimalarial which differs from quinacrine chlorguanide and pyrimethamine in that it acts on the gametocytes of all the causative agents of malaria including the "crescents of tropical malaria" In 1—2 days after the administration of the drug, the gametocytes lose the ability to infect the mosquito and in 4—5 days disappear completely from the blood Thanks to its ability to act to some extent on the tissue forms of the plasmodia, methoxy diethylaminopropylamino quinoline used in conjunction with schizontropic drugs (quinacrine, chlorguanide and quinine) reduces the percentage of relapses

Methoxy diethylaminopropylamino quinoline is not used alone it is an ingredient of tablets containing quinacrine and chlorguanide

Maximal doses for adults single—0.04 g, daily—0.06 g

Maximal doses for children 2 years old, single—0.005 g, daily—0.01 g 3—4 years single—0.0075 g daily—0.015 g 5—6 years single—0.01 g daily—0.02 g 7—9 years single—0.015 g daily—0.03 g 10—14 years single—0.02—0.025 g daily—0.04—0.05 g The drug is not prescribed for infants up to 1 year old

Overdosage of methoxy diethylaminopropylamino quinoline leads to side effects in the form of headache and epigastric pain paresthesia and neuralgic pains in the region of the trigeminal nerve, gross overdosage causes cerebellar ataxia polyneuropitis and atrophy of the optic nerve

At the first symptoms involving the nervous system, the administration of the drug must be discontinued immediately, stomach lavage performed and large

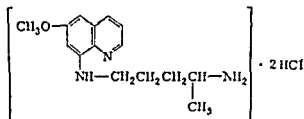
amounts of fluid administered caffeine is prescribed and if necessary, 0.1% atropine solution is injected retrobulbarly the prescription of vitamin B₁, nicotinic acid and liver preparations is beneficial

Contraindications 1) diseases of the fundus and the optic nerve, 2) encephalitis meningoencephalitis or a past history of these diseases 3) past history of toxic reactions following the administration of the drug

To be kept locked (List A) in well stoppered bottles of dark glass if the drug has changed in appearance it is unfit for use

CHINOCID (Chinocidum)

6-Methoxy-8-(4'-aminopentyl)-aminoquinoline dihydrochloride



Light yellow fine crystalline powder bitter taste, freely soluble in water (1:2) soluble in alcohol (1:50) insoluble in ether Decomposes under the influence of moisture

Chinocid is closely related to methoxy diethylaminopropylamino quinoline in chemical structure both being derivatives of 8-aminoquinoline Chinocid is effective against the tissue forms of malaria plasmodia and can prevent relapses within short or long periods of time of 3-day malaria with a short incubation and relapses within a short period of time of the same form of malaria having a long incubation

Chinocid is used to prevent relapses of 3-day malaria and also for pre-epidemic chemo prophylaxis It has a weaker action against the erythrocyte forms of malaria plasmodia and is not used for the treatment of acute malarial attacks

Acute attacks of malaria are treated by the administration of chloroquine or chloroquine and methoxy diethylaminopropylamino quinoline for 5 days if these drugs are not available quinine or quinacrine and methoxy aminopropylamino quinoline are used instead Chinocid can be prescribed as soon as the administration of schizontocides has been discontinued

Chinocid is given orally after meals in a daily dose of 0.03 g for adults, 1-2 administrations a day for 10 days (Schedule 1) or in a daily dose of 0.02 g for 14 days (Schedule 2)

Children are also given chinocid for 10 or 14 days in the following doses

Age	Daily dose, g	
	Length of treatment	
	10 days (Schedule 1)	14 days (Schedule 2)
Up to 1 year	0.0025	0.0015
1-2 years	0.005	0.0025
3-4 "	0.0075	0.005
5-7 "	0.01	0.0075
8-12 "	0.015	0.01
13-15 "	0.02	0.015
Over 15 "	0.03	0.02

The drug is given in 1—2 doses after meals

Treatment is carried out according to Schedule 2 in severe forms of the disease in weakened patients, and preferably on an in patient basis

Patients who have completed the course of treatment for acute attacks and the course of chinocid administration are freed in future from public chemo prophylaxis

For the pre-epidemic chemo prophylaxis of 3 day malaria having a long incubation period, in persons who contracted the disease the preceding season of transmission, chinocid is prescribed not later than a month before the period of the mass appearance of fresh cases, adults are given 0.03 g daily for 10 days

Side effects may occur when chinocid is taken nausea, headache, and cyanosis of the lips and finger nails In isolated cases there may be symptoms of irritation of the kidneys and bladder, as well as drug fever, slight hemolysis, leukopenia or leukocytosis may be observed Side effects pass away when the drug is withdrawn

Relative contraindications diseases of the blood and hemopoietic organs, kidney diseases and stenocardia

Chinocid must not be prescribed simultaneously with other antimalarials as this increases the toxicity

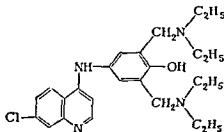
Caution must be observed in prescribing chinocid for aged and weak patients

Available in powder form and in dragees of 0.005 and 0.01 g

To be stored in hermetically sealed vials of dark glass in a dry place protected from light observing safety precautions (List B)

CYCLOCHIN (Cyclochunum)

7 Chlor-4-[3,5' bis (diethylaminomethyl) 4' hydroxyphenyl] aminoquinoline



Yellow crystalline substance, bitter taste, insoluble in water, readily soluble in dilute acids, insoluble in dilute alkalis Melting point 164—165°

Cyclochin acts on the erythrocyte forms of all types of malaria Its administration in acute cases of malaria leads to the cessation of fever and the elimination of parasitemia, it is especially indicated in cases of tropical malaria resistant to chloroguanide

Cyclochin is administered orally The dose for adults is 0.3 g once a day (in the morning after a light breakfast), prescribed 3 days in succession — 0.9 g for the course In order to obtain a quicker cessation of acute manifestations of malaria, a 2 day course of treatment may be given 0.3 g twice the first day (with a break of 6 hrs between doses), and a single dose of 0.3 g the second day

Children are prescribed cyclochin once a day in the following doses up to 1 year old — 0.025 g, 1—2 years — 0.05 g, 2—4 years — 0.075 g, 4—6 years — 0.1 g, 6—8 years — 0.15 g, 8—12 years — 0.15—0.2 g, 12—16 years — 0.25 g

There may be relapses of 3 day malaria in 1½—2 months after the course of treatment with cyclochin To prevent relapses and obtain a radical cure of 3 day malaria chinocid should be prescribed 24 hrs after ceasing administration of cyclochin adults are given 0.02 g once a day for 14 days The simultaneous

administration of cyclochin and chinocid is contraindicated because of the possibility of toxic symptoms (see Chinocid)

For individual prophylaxis cyclochin is administered in a dose of 0.3 g (for adults) once a week during the epidemic season

For the pre epidemic prophylaxis of malaria in persons living in places where infection with 3 day malaria of long incubation period is possible cyclochin is given in a dose of 0.3 g for 3 days followed by 0.02 g chinocid for 11 days (for adults)

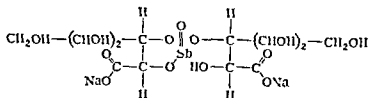
Available in powder form and in tablets of 0.3 g (for adults) and 0.05 g (for children)

To be stored in a place protected from light observing safety precautions (List B)

b) Drugs for the treatment of leishmaniasis amoebiasis trichomoniasis and Other Protozoan Infections¹

SOLUSURMIN (Solusurminum)

Sodium salt of pentavalent antimony gluconic acid complex



Contains 21—23% antimony

An analogous preparation is put out abroad under the names Natrium stibio gluconicum Sodium antimonyl gluconate Triostam

White powder soluble in water insoluble in organic solvents Aqueous solutions are sterilized by holding at 100° for 30 min

Has a chemotherapeutic action in visceral and dermal leishmaniasis

Administered intravenously intramuscularly and subcutaneously in the form of a 5% solution Only freshly prepared sterile solutions are used for injections Daily injections are given Course of treatment 20—30 injections If there should be a relapse of the disease treatment can be repeated

Treatment of adults is begun with the administration of 3 ml 5% solution gradually increasing the dose 16 ml daily up to 8—10 ml a day Children are given the following doses depending on their age

Age	1st injection	2nd injection	3rd injection	4th and following injections
	ml 5% solution			
Up to 1 year	1—1.5	1.5—2	2—2.5	3—3.5
1—3 years	1.5—2	2—2.5	3—3.5	4—5
3—6 "	2—2.5	3—3.5	4—4.5	5—6
7—10 "	2.5—3	4—4.5	5—5.5	6—7
11—15 "	3	4.5—5	5.5—6	6.5—7.5

A method has likewise been proposed for treatment with large doses of solusurmin which makes it possible to reduce the length of treatment and gives

¹ See also Antibiotics Alliglycer Q nacrine Amibiquinacrine Acetarsone

d results (N A Mirzoyan) According to this method 10–20% solutions are prepared with twice distilled water they can be kept for 2–3 days but if the slightest turbidity should appear they are no longer fit for use (20% solution is slightly opalescent immediately after preparation)

Solutions are injected intravenously If necessary they can be injected subcutaneously but this method of administration may be painful and in some cases thromboses develop

According to this method the drug is administered intravenously and subcutaneously in the following doses

Patients' age and condition	Dose g per kg body weight			Length of treatment days
	1st injection	2nd injection	3rd and following injections	
0 to 7 years old, no dystrophic changes	0.03	0.1	0.15	10–12
0 to 7 years old dystrophic changes or other concurrent diseases	0.04	0.08	0.12	14–15
7–14 years	0.04	0.07	0.12	12–14
Over 14 years	0.04	0.07	0.1	14–16

Children are given 1 injection daily adults — 2 injections (morning and evening) In cases that respond poorly to treatment the daily dose after 7–10 injections is increased to 0.15 g per kg body weight for children and 0.12 g per kg body weight for adults The length of the course depends on the effectiveness of treatment If the effect achieved in the time indicated is insufficient the course of treatment is lengthened but not more than to 20–22 days If there should be an earlier normalization of the temperature a substantial improvement in the composition of the blood disappearance of leishmania from the bone marrow and normalization of the patients' condition the administration of solusurmin is discontinued

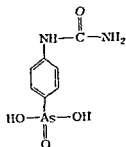
Solusurmin is usually tolerated well and breaks should not be made in treatment

Available in powder form in hermetically closed vials

To be stored in the original package in a place protected from light observe safety precautions (List B)

CARBARSONE (Carbarsonum)

p Carbamidophenylarsonic acid



Contains 28.3—29.3% arsenic

Synonyms Ameban Amebarson Amebevan Ambiarson Aminarson Carbazon Fenarson Leucarson

White crystalline powder sparingly soluble in cold water (1:170) more soluble in warm water (1:30) readily soluble in solutions of caustic alkalis and carbonates of alkali metals. Aqueous solutions have an acid reaction. Melting point 172—174°

Used in the treatment of amoebiasis balantidiasis and trichomonadal vaginitis and at times in infestation of the intestine with *Trichomonas*

In amoebic dysentery and balantidiasis the drug is administered to adults in a dose of 0.25 g 3 times a day for 10 days (or in 2 cycles of 5 days treatment followed by a break of 5 days) after 10 days the cycle of treatment can be repeated. Children are prescribed the following doses

Age	Daily dose g
Up to 6 months	0.12
From 6 months to 1 year	0.21
1—2 years	0.3
2—3	0.4
3—5	0.4—0.5
5—8	0.5
8—12	0.5—0.75
12—16	0.75

These doses must not be exceeded

Maximal doses for adults single — 0.25 g daily — 1 g

In acute cases of amoebic dysentery carbarsone can be administered in conjunction with emetine

In trichomonadal vaginitis carbarsone is applied in the form of vaginal suppositories of 0.12 g. Treatment is carried out for a period of 2 weeks

Contraindications diseases of the liver and kidneys acute gastrointestinal disorders ulcer of the stomach and duodenum dermatitis disturbances of circulation hemorrhagic diathesis severe forms of diabetes and tuberculosis pregnancy past history of intolerance for arsenicals

Side effects may occur during treatment with carbarsone such as dermatitis irritation of the kidneys elevated temperature nausea vomiting diarrhea and icterus

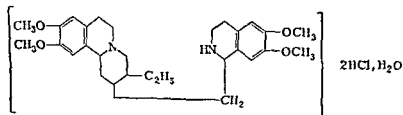
If side effects should develop the dose is reduced or a break made in treatment or the drug withdrawn completely

Available in powder form and in tablets of 0.25 g

To be kept locked (List A) in well stoppered bottles of amber glass

EMETINE HYDROCHLORIDE (Emetinum hydrochloricum Emetini hydrochloridum)

Hydrochloride of the alkaloid emetine contained in the bark of *ipeacuanha*



White or slightly yellowish crystalline powder odourless bitter taste freely soluble in water (1:8) and alcohol pH of 1% solution = 4.5—6.0 Aqueous solutions are sterilized by holding at 100° for 30 m

Has a chemotherapeutic action against the causative organism of amoebic dysentery, and to a certain extent, against some trematodes

In amoebic dysentery emetine hydrochloride is administered subcutaneously or intramuscularly in a dose of 15 ml 2% twice a day (for adults)

Maximal doses for adults, subcutaneously and intramuscularly single — 0.05 g daily — 0.1 g

Doses for children are reduced according to their age

Age	Daily dose, g
From 6 months to 1 year	0.005
1—2 years	0.01
2—5 "	0.02
5—9 "	0.03
9—15 "	0.04

These doses must be exceeded. Infants up to 6 months old are not prescribed emetine

Duration of treatment 4—6 days maximum 7—8 days. When the stool has become normal or semi normal in consistency administration of emetine is stopped, and chiniofon given instead. The total dose of emetine for the course of treatment should not exceed 0.01 g (10 mg) per kg body weight, in the overwhelming majority of cases, a considerably smaller amount will suffice. As a rule emetine is prescribed only when there are acute intestinal symptoms. Because of the cumulative properties of emetine treatment must not be repeated before a lapse of at least 7—10 days.

When treatment with emetine is instituted at the first acute symptoms of amoebic dysentery one or two cycles are usually sufficient. In protracted forms the number of cycles is increased to 3 or 4. Antibiotics and other antibacterial drugs can be administered simultaneously. Combined treatment with emetine and carbarsone is also recommended.

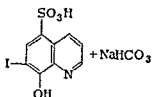
During treatment with emetine (particularly if there is an overdosage) side effects may occur: weakness, nausea, vomiting, pains in the muscles of the extremities, cardiac weakness and polyneuritis. If there should be pronounced side effects, treatment with emetine must be stopped.

Available in powder form and in ampoules containing 1 ml 1% solution.

To be stored in well stoppered bottles in a place protected from light, observing safety precautions (List B).

CHINIOFON (Chiniofonum)

A mixture of 8-hydroxy-7-iodoquinolinesulfonic acid and sodium bicarbonate in the proportion of 3 : 1.



Synonyms Anayodin, Avlochin, Besomin, Chinosulfan, Iochinolum, Loretin, Myxioide, Quinoxyl, Rexioide, Triven, Yavion, Yatren.

Yellow powder, odourless, soluble in 30 parts of water with the evolution of carbon dioxide, insoluble in organic solvents. Contains about 25—26% iodine. Solutions for injections are prepared with distilled water that has been freshly boiled and cooled to 80°.

Used in amoebic dysentery and ulcerous colitis and at times in acute and chronic articular and muscular rheumatism, suppurating wounds, burns etc.

Administered orally and parenterally in amoebic dysentery and ulcerous colitis applied locally in the form of 0.5–3% solutions 5–10% ointments and 10% dusting powder for the treatment of suppurating wounds ulcers and burns as well as in gynecology and urology. In amoebic dysentery adults are given a dose of 0.5 g 3 times a day the dose can gradually be increased to 3 g per day. The cycle of treatment is for 8–10 days (or two 5 day cycles of treatment can be given with a break of 5 days between). Treatment can be repeated after a 10 day break. Children are given the following doses

Age	Daily dose g
From 1 year to 2 years	0.1
2–3 years	0.15
3–4	0.2
From 4–5 years	0.25
5–6	0.3
6–8	0.45
8–12	0.6
12–13	0.7
13–15	1
16 and older	1.5

Chinifon can also be administered in enemas 200 ml 1–2% solution in warm water after a cleansing enema (for adults)

In the presence of acute symptoms chinifon can be used in conjunction with emetine. In protracted cases it is advisable to prescribe carbarsone or actarson simultaneously.

In acute and chronic articular and muscular rheumatism chinifon is sometimes administered in the form of intramuscular or subcutaneous injections of 5 ml 5% solution.

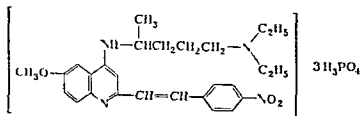
Maximal doses for adults single — 1 g daily — 3 g

Available in powder form and in tablets of 0.5 g

To be stored in a dry dark place in bottles of amber glass with ground glass stoppers, observing safety precautions (List B)

TRICHOMONACID (*Trichomonasacidum*)

6-Methoxy-2-(4-nitrostyryl)-4-(α -methyl- δ -diethylamino) butylaminoquinoline triphosphate



Yellow crystalline powder freely soluble in water and alcohol. Melting point 158–160°

Highly active against *Trichomonas*. Used in males and females for the treatment of genitourinary diseases caused by *Trichomonas vaginalis*.

Administered locally and by mouth. Orally adults are given 0.3 g daily (2–3 doses after meals) for 3–5 days. For children the dose is reduced according to their age. In men 10 ml 1% trichomonacid solution is simultaneously introduced into the urethra for 10–15 min over a period of 5–6 days. The course of treatment can be repeated in 10–20 days.

In women simultaneously with oral administration the drug is applied to urethra bladder and rectum on the 1st day to the cervix on the 4th day to the cervix urethra bladder and rectum (after natural evacuation) on the 8th day and to the cervix on the 12th day The drug is applied to urethra bladder (after evacuation) and rectum in the form of a 0.25–0.5% suspension in liquid petrolatum 10 ml being introduced by means of a syringe and rubber catheter If there are no unpleasant sensations it is advisable to refrain from urination for 2–3 hrs after application to the urethra and bladder Trichomonacid is introduced into the cervical canal in the form of 0.025 or 0.05 g tablets or powder In the intervals between procedures which should be carried out by a physician on an out patient basis the patient should introduce a globule containing 0.05–0.1 g of the drug into the vagina every night before retiring (after toilet) for a period of 10 days Treatment is carried out after the end of menstruation during 3 ovarian cycles

In pregnant women suffering from nausea and vomiting treatment may be limited to the application of globules containing 0.05 g of the drug over a period of 10 days

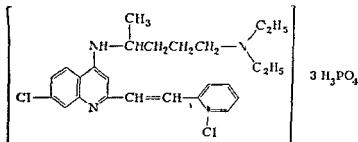
In large doses and high concentrations trichomonacid may have an irritating effect on the mucous membranes In women there may be copious discharges after administration and unpleasant sensations in the region of the vagina these symptoms pass away when the drug is withdrawn or the dose reduced In men there may be copious discharges from the urethra in such cases instillation is temporarily stopped

Available in powder form and in tablets of 0.025 0.05 and 0.1 g

To be stored under ordinary conditions observing safety precautions (List B)

AMINOCHINOL (Aminochinolum)

7 Chloro 4 diethylaminoisopentylamino 2 (2 chlorostyryl) quinoline triphosphate



Yellow crystalline powder odourless bitter taste soluble in water and alcohol Melting point 196–198° (with decomposition)

Has a chemotherapeutic effect in some protozoan infections used for treatment of lamblasis as well as lupus erythematosus

In lamblasis the drug is administered in cycles of 5 days with a break of 4–7 days between Usually two cycles of treatment are given if the effect is inadequate 3 cycles are carried out Administered orally half an hour after meals The dose for adults is 0.15 g 2–3 times a day Daily doses for children up to 1 year old—0.025 g 1–2 years—0.05 g 2–4 years—0.075 g 4–6 years—0.1 g 6–8 years—0.15 g 8–12 years—0.15–0.2 g 12–16 years—0.25–0.3 g The daily dose is given in 2–3 administrations

In discoid lupus erythematosus aminochinol is administered orally in a dose of 0.1 g for adults 2–3 times a day in cycles of 10 days with a break of 5 days between

Aminochinol is usually tolerated well unlike quinacrine it causes no colouring of the skin In isolated cases there may be nausea and headache If there

should be allergic skin reactions administration must be discontinued During treatment watch must be kept on the functions of the liver and kidneys and on the blood picture

Available in powder form and in tablets of 0.025 0.05 0.1 and 0.15 g

To be stored in tightly closed bottles in a dry place protected from light observing safety precautions (List B)

SANAZIN (Sanazinium)

Synthetic antibiotic similar in structure to pyocyanine.

Dark blue crystalline powder soluble in water alcohol glycerol and a number of organic solvents

Has antimicrobial activity against pyogenic cocci the causative agents of diphtheria whooping cough and tuberculosis dysentery and typhoid bacilli *Brucella Trichomonas* and other microorganisms

Sanazin was proposed for the treatment of tuberculosis of the eyes and bones and joints. Lately however since more effective drugs have been obtained for the treatment of tuberculosis sanazin has been used for the following purposes: a) treatment of diseases caused by *Trichomonas* b) local treatment of suppurative inflammatory processes in the presence of flora sensitive to sanazin c) treatment of diphtheria and streptococcal bacilli carriers as well as the treatment of patients with whooping cough in the early stages of the disease d) treatment of acute and chronic dysentery (in conjunction with levomycetin synthomycin or other antibiotics and also with vaccinotherapy)

Sanazin is administered orally locally and in the form of enemas

In treating trichomoniasis in males and females sanazin is administered orally in a dose of 30 ml 0.1% solution 5 times a day. In women vaginal packs moistened with a glycerol solution of the drug are also used. A 1% solution of sanazin on glycerol is prepared with the addition of 4% sodium bicarbonate. For irrigation of the bladder 100—200 ml of 0.1% aqueous solution is used. Enemas are likewise used 30 ml 1:300 solution with the addition of 5 g sodium bicarbonate. The course of treatment is for 10—15 days after a month's rest a second course of treatment is given (10—15 days).

Sanazin is used locally for irrigating wounds and cavities in the form of a 0.05—0.2% aqueous solution; it is applied in conjunctivitis and blepharitis in the form of a 0.1% ointment.

In diphtheria carriers a 0.2—0.4% aqueous or alcoholic glycerol solution is used for swabbing the mucosa of the nasopharynx. The pharynx is swabbed with a cotton plug twice a day for 7 days.

In dysentery sanazin is used in conjunction with antibiotics (levomycetin synthomycin or others) administered orally in the form of a 0.1% aqueous solution (adults 30—40 ml 4—6 times a day children 5—20 ml), and in enemas (adults 50—100 ml 0.1% solution twice a day children 10—30 ml). Antibiotics are given according to the usual schedules but in smaller doses (approximately $\frac{1}{2}$).

Sanazin is contraindicated in malignant and tuberculous allergic (phlyctenular) forms of ocular diseases.

During treatment careful watch must be kept on the blood picture. If myelocytes and young forms should appear or marked eosinophilia and a sharp acceleration of the sedimentation rate and patients should feel bad the dose must be reduced or treatment discontinued.

Available in powder form

Sterile 0.05—0.2% aqueous solutions are prepared by dissolving the necessary amount of the drug in boiling twice distilled water after cooling the solution is filtered through a paper filter and sterilized by holding in the autoclave for 20 min at a temperature of 110°.

Sanazin can be dissolved more easily by triturating in a mortar with 96% alcohol and then dissolving in 0.1% sodium bicarbonate solution. After heating on the water bath 20—30 min the solution is cooled filtered and poured into

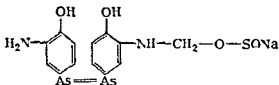
bottles Solutions of sanazin in sodium bicarbonate and glycerol are only for local use When preparing glycerol solutions the drug is first triturated in a mortar, and the necessary amount of glycerol and sodium bicarbonate then added (4 g per 100 ml glycerol)

E Antisyphilitic drugs¹

a) Organic arsenicals

NOVARSENOL (Novarsenolum)

Mixture of sodium 3,3'-diamino-4,4'-dihydroxyarsenobenzene methanalsulfoxylate and 3,3'-diamino-4,4'-dihydroxyarsenobenzene dimethanalsulfoxylate



Sodium 3,3'-Diamino-4,4'-dihydroxyarsenobenzene methanal sulfoxylate

Analogues Neosaminol Nearsemin Novarsenobillon Neosphenamin Neosalvarsan Neotreparsenan Novarsan Novarsenobenzene Revival Rhodarsan Spirosonovan

Loose yellow powder freely soluble in water with the formation of a transparent yellow solution of neutral or weakly alkaline reaction Contains 19–20% arsenic

Novarsenol is one of the principal organic arsenicals which have a high chemotherapeutic activity in spirochetoses and some diseases caused by protozoa

According to modern conceptions the mechanism of the therapeutic action of these drugs consists in their ability to block the sulfhydryl (thiol) enzymatic systems of the microorganisms in this way upsetting the metabolic processes in their organism

Novarsenol is chiefly used for the treatment of syphilis

Available in powder form and in sealed ampoules containing 0.15 0.3 0.45 and 0.6 g

Before using novarsenol or myarsenol (see below) the ampoule must be carefully examined If there should be a crack in the glass or if the drug has changed colour it is unfit for use The drug should pour freely within the ampoule without adhering to the walls and without forming lumps it should be coloured uniformly in the usual tint and should dissolve freely If the drug should deviate from the normal and there is doubt as to its quality, another ampoule should be used

Novarsenol is dissolved in distilled freshly sterilized water at room temperature Whatever the dose, the drug is dissolved in 5–6 ml water When dissolving the drug it is sprinkled over the entire surface of the water and carefully stirred with a glass rod Vigorous shaking and stirring is not advisable Novarsenol solution should be absolutely transparent

Novarsenol solution is prepared separately for each patient and is used immediately When solutions stand 5 min or more in the air they undergo considerable oxidation and become unfit for use Novarsenol solution is injected intravenously The injection should be given slowly — over a period of 1–2 min It is not advisable to administer novarsenol sooner than 2–3 hrs after meals the

¹ See also Penicillin Mercuric cyanide Mercuric chloride Drugs containing iodine

next meal should be in 2—3 hrs after the injection. When treating syphilis it is advisable to precede the first administration of novarsenol with 1—3 injections of mercury or bismuth drugs.

In the absence of contraindications the initial dose of novarsenol is 0.3 g for men and 0.15 g for women. It is recommended that the dose for subsequent injections should be raised 0.15 g each time but the dose for men should not exceed 0.6 g per injection and that for women should not exceed 0.45 g. The drug is administered at the rate of 0.1—0.12 g daily with the proper breaks between injections.

A daily dose of 0.12 g is only used in somatically healthy people weighing at least 60 kg; in other patients the daily dose should not exceed 0.1 g.

The total dose for the course of treatment in primary and secondary syphilis is 7—5.5 g for men and 1.5—5 g for women. In tertiary forms the daily dose should not exceed 0.1 g and the total dose for the course should not exceed 3—4 g.

In syphilis of the nervous system the total dose for the course should not exceed 5 g for men or 4.5 g for women.

The use of smaller single or total doses or prolonging treatment for longer periods is not recommended.

Maximal dose intravenously for adults 0.6 g (once in 3—5 days).

In treating children the following table is used as a guide.

Age	Dose for one injection g	Total dose for course of treatment, g
Up to 6 months	0.03—0.15	0.8—1.0
From 6 months to 1 year	0.05—0.15	1.0—1.25
1—3 years	0.05—0.2	1.5—2.0
3—5 "	0.1—0.25	2.0—2.5
5—10 "	0.1—0.3	2.5—3.0
10—15 "	0.1—0.3	3.0—3.5

The first injection should be with the minimum dose for the age. Injections are given once in 5 days.

Serious complications following the administration of novarsenol such as disseminated dermatitis, icterus and polyn neuritis require the immediate cessation of treatment with arsenicals for a lengthy period; in future special care must be observed in setting the dosage.

If there should be erythema or syndrome of the 9—12th day treatment must be discontinued and should not be resumed sooner than 8—10 days after the complete disappearance of symptoms. Treatment should be commenced with reduced doses gradually raising them to the usual amount. If there are mild or complications the next administration of the drug is given in a somewhat smaller dose and after the patient's general condition has been fully restored.

Absolute contraindications: individual intolerance for such drugs; acute gastrointestinal diseases; ulcer of stomach and duodenum in stage of exacerbation; serious nonsyphilitic diseases of the central nervous system; severe nonsyphilitic affections of the liver; disseminated acute inflammatory diseases of the skin; severe nonsyphilitic affections of the kidneys; diabetes that is unresponsive to diethotherapy; heart disease in stage of decompensation; persistent disturbances of rhythm; pronounced forms of hypertensive disease; hemorrhagic diathesis and other serious disturbances of hemopoiesis; serious forms of pulmonary tuber-

culosis and all cases of hemophysis pronounced forms of exophthalmic goiter myxedema Addison's disease acute infectious diseases ocular diseases (non specific iritis iridocyclitis keratitis chorioretinitis affections of the optic nerve)

The administration of novarsenol after infectious diseases is impermissible before at least 5—6 days have elapsed since the temperature has fallen to normal and on condition that all symptoms of the disease have disappeared and the patient again feels well in general

Relative contraindications requiring caution in the use of novarsenol age over 50 years chronic intoxication (alcoholism drug addiction lead poisoning etc) cardiovascular diseases cachexia tuberculosis of lungs nose throat and larynx severe forms of anemia diseases of the central nervous system accompanied by degenerative changes epilepsy of nonsyphilitic etiology affections of larynx accompanied by difficult breathing pronounced tonsillitis otosclerosis diseases of liver and kidneys or past history of such diseases exophthalmic goiter obesity Meniere's disease

Pregnancy is not a contraindication to the treatment of syphilis with arsenicals but the single dose of novarsenol should not be higher than 0.4 g and the total dose for the course should not exceed 4—4.5 g

Novarsenol is also used for the treatment of relapsing fever sodoku Plaut—Vincent's angina abscess and gangrene of the lungs and some other diseases

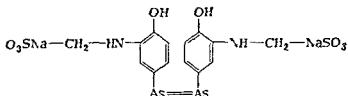
In relapsing fever men are given 2—3 injections of 0.45 g intravenously at intervals of 4—6 days the dose for women is 0.3 g In sodoku 4 injections of 0.45—0.6 g are given at intervals of 5 days In Plaut—Vincent's angina in cases of considerable necrosis in the pharynx 0.3—0.4 g novarsenol is administered twice the second time—48 hrs after the first In abscess and gangrene of the lungs novarsenol is injected intravenously beginning with a dose of 0.15 g if tolerance is good another 0.3 g is given in 2 days and 0.4 g 3 days later 0.45 g is given 2—3 times more at intervals of 5 days

In gingivitis and ulcerous stomatitis accompanied by fusospirochloetosis a 10% suspension of novarsenol in glycerol is applied topically

To be kept locked (List A) in sealed ampoules in a cool place protected from light

MYARSENOL (Myarsenolum)

Disodium 3,3'-diamino-4,4'-dihydroxyarsenobenzene N,N'-dimethylenesulfonate



Analogous drugs are marketed abroad under the names Myoarsemin Myoarsarsan Sulfarsenol Sulfarsphenaminum Sulfostab Thioarsamin

Pale yellow light amorphous powder very freely soluble in water insoluble in alcohol and ether Contains 18.2—19.2% arsenic

Available in ampoules containing 0.15 0.3 0.45 and 0.6 g

Use late forms of syphilis poor tolerance for novarsenol pediatric practice final courses in the treatment of primary syphilis cases in which there are difficulties in giving intravenous injections of novarsenol Myarsenol can also be used for the first course of treatment

Myarsenol is injected intramuscularly in the outer upper quadrant of the buttocks with a 5—6 cm needle The drug is dissolved in 1.5—2 ml sterile freshly distilled water at room temperature irrespective of the dose For patients

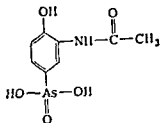
with heightened sensitivity to pain, myarsenol can be dissolved in the same amount of 1% procaine hydrochloride solution. Solutions must be absolutely transparent. Solutions are prepared separately for each patient immediately before use. Injections should be made slowly. Administered 2–3 hrs before or 2–3 hrs after meals.

Single and course doses of myarsenol, possible complications and contraindications are the same as for novarsenol.

To be kept locked (List A) in sealed ampoules in a cool place, protected from light.

ACETARSONE (Acetarsonum).

4-Hydroxy-3-acetylaminophenylarsonic acid



Synonyms: Acetarsolum, Acetphenarsin, Amarsan, Arsaphen, Devegant, Dynarson, Kharophen, Kubarsol, Lmarsol, Nilacid, Orarsan, Orvarsan, Osar sol, Pallicid, Spirocid, Stovarsol, Vagival.

Fine white crystalline powder, forming lumps, odourless, very sparingly soluble in water and alcohol, soluble in sodium bicarbonate solution and in solutions of caustic alkalis and ammonia. Contains about 27% arsenic.

Use: manifestations of late syphilis, syphilitic diseases of the cardiovascular and nervous systems, last courses in the treatment of secondary and tertiary syphilis. Can also be used for treating syphilis in children. Acetarsonum is convenient for use since it is administered orally, however, for treating fresh forms of syphilis, it is novarsenol or myarsenol of the arsenicals that is used. Acetarsonum is likewise used in combination with bismuth and mercury drugs and penicillin; the simultaneous prescription of other arsenicals is impermissible.

Acetarsonum is likewise used in treating trichoccephaliasis, amoebic dysentery and trichomonadal colitis.

In treating patients with syphilis, acetarsonum is administered in cycles of 5 days with a 3-day break between.

Adults are given acetarsonum in 0.25 g tablets according to the following schedule:

1st day	— 1 tablet (0.25 g)	in the morning 1 hr before breakfast
2nd "	1 " (0.25 g)	" " evening 1 hr " " and
	1 " (0.25 g)	" " evening 1 hr " " supper
3rd "	2 " (0.5 g)	" " morning 1 hr " breakfast and
	1 " (0.25 g)	" " evening 1 hr " supper
4th–5th day	2 tablets (0.5 g)	in the morning 1 hr before breakfast and
	2 " (0.5 g)	" " evening 1 hr before supper

After 5-day treatment a break of 3 days is made, after which 2 tablets (0.5 g) are given morning and evening 1 hr before meals, after 5 days, another 3-day break is made, and the cycle of treatment again repeated. The total dose for an adult for the course of treatment is 30–40 g.

Children are given acetarsonum in the following doses according to their age.

Age	Single dose, g	Daily dose, g	Total dose for course, g
1-6 months	0.06	0.12	4
6 months - 1 year	0.12	0.24	6
1-2 years	0.14-0.2	0.3-0.4	8
2-5 "	0.25	0.5	10
5-8 "	0.25	0.5	15
8-12 "	0.25-0.5	0.5-0.75	20
12-16 "	0.25-0.5	0.75	25
Over 16 "	0.25-0.5	0.75-1	30

In amoebic dysentery (during a period of remission), adults are given 0.25 g 3 times a day before meals, for 3 days a 4 day break is then made, after which the cycle of treatment can be repeated.

In the treatment of trichocephaliasis acetarsone is administered to adults in a dose of 0.25 g according to the following schedule 1st 2 days - 3 times a day an *hr* before meals, 3rd - 5th days - 4 times a day an *hr* before meals. On the 6th day a salt laxative is given. During the 5 days a total of 18 tablets is given.

Acetarsone is not used as an anthelmintic for children up to 6 years old. For older children the total number of tablets given during the course of treatment (5-6 days) is equal to their age in years. The daily dose is given in 3-4 administrations, the 0.25 g tablets being divided ($\frac{1}{4}$, $\frac{1}{3}$ or $\frac{1}{2}$).

In the treatment of trichomonadal colpitis a mixture of 0.25 g acetarsone and 0.25 g boric acid is introduced into the vagina, the powder being evenly distributed over the walls. The speculum is then extracted and the urethra swabbed with 1% silver nitrate solution. This procedure is carried out once a week. The vagina is swabbed once more each week and the mixture of acetarsone and boric acid applied. If *Trichomonas* is found in the rectum, suppositories containing 0.25-0.3 g acetarsone and boric acid are prescribed, they are applied once a day, after evacuation, for 10 days (S. K. Lesnoi). Pellets containing acetarsone, boric acid and glucose, 0.3 g each (Osarbon), can also be used for the treatment of trichomonadal colpitis. Pellets containing acetarsone, boric acid, glucose and sulfanilamide 0.3 g each (Osarcid) are likewise available.

Maximal doses of acetarsone, orally, for adults single - 0.25 g daily - 1 g. Doses for children in the treatment of syphilis should not exceed those specified in the preceding table.

Maximal doses for children as an anthelmintic 5-6 years old single - 0.08 g, daily - 0.25 g, 7-9 years, single - 0.125 g, daily - 0.375 g, 10-14 years, single - 0.2 g, daily - 0.6 g.

When prescribing acetarsone, a preliminary analysis of the urine for albumin must be made. If albumin is present, acetarsone is contraindicated. Other contraindications: diseases of the liver, severe forms of diabetes, heart disease, acute gastrointestinal disorders, severe forms of tuberculosis, hemorrhagic diathesis, dermatitis, nonsyphilitic diseases of the optic and auditory nerves, ulcer of the stomach and duodenum, menstruation and pregnancy.

Complications: neuritis, dermatitis, irritation of the kidneys, elevated temperature, nausea, vomiting, diarrhea and icterus.

Available in powder form and in tablets of 0.25 g.

To be kept locked (List A) in well stoppered bottles of dark glass.

b) Bismuth preparations

BIIOCHINOL (Bilochinololum)

8% suspension of bismuth quinine iodide in neutral vegetable oil 1 ml contains 0.02 g metallic bismuth

After thorough shaking the suspension is of a uniform brick red colour on standing a brick red sediment forms

Bilochinol is an active antisyphilitic preparation and is used in treating all forms of syphilis. Likewise because of its antiphlogistic and resolvent properties it is used for the treatment of nonsyphilitic affections of the central nervous system: arachnoencephalitis meningomyelitis sequelae of impaired cerebral circulation etc

Bilochinol is injected intramuscularly in the upper outer quadrant of the buttocks by means of a long needle. After the needle has been introduced a check must be made to see whether blood appears in the cannula; it is only after the absence of blood has been established that the syringe is attached and the preparation slowly injected. Before administration the vial is warmed in hot water (not higher than 40°) and thoroughly shaken. In the treatment of syphilis, adults are usually given an injection of 3 ml once in 3 days. Total preparation for the course 10-30 ml. In the treatment of nonsyphilitic affections of the nervous system daily injections of 1 ml are given.

Maximal single dose for adults intramuscularly 3 ml (once in 3 days). Children are given injections once in 3 days in the following doses:

Age	Dose per injection ml	Total dose for course ml
Up to 6 months old	0.3-0.5	8
From 6 months to 1 year	0.5-0.8	10
1-3 years	0.5-1	12-15
3-5 "	1-1.5	15-20
5-10 "	1-2	20-30
10-15 "	1-3	25-30

Side effects rarely occur when the usual dosage and the correct injection technique are used. In isolated cases as when treating with other bismuth preparations the so called "bismuth border" is observed—a slate coloured border along the gum line and around some teeth especially those that are carious. If the mouth is cared for properly the bismuth border rarely occurs.

Contraindications: kidney disease, diabetes, hemorrhagic diathesis, advanced stages of tuberculosis, decompensated cardiac activity, gingivitis, stomatitis, amphodontosis and heightened sensitivity to quinine. During treatment the mouth must be kept clean and watch must be kept on the condition of the liver and kidneys. If albumin casts or bismuth cells should appear in the urine or gingivitis or stomatitis set in a break must be made in treatment.

Available in vials containing 100 ml

To be stored in the original package in a cool dry place observing safety precautions (List B)

BISMOVEROL (Bismoverolum)

Suspension of basic monobismuth tartrate in neutral persic oil

When shaken the preparation forms a white suspension on standing a white sediment settles out. 1 ml contains 0.05 g metallic bismuth.

Used for treating syphilis (in all periods) Injected intramuscularly in the upper outer quadrant of the buttocks injections are almost painless Adults are given doses of 1 ml each second day during the first half of the course of treatment and each third day during the second half of the course The total dose for the course is 16–20 ml of suspension the equivalent of 0.8–1 g metallic bismuth

Maximal doses for adults intramuscularly 1 ml (once in 2 days)
When treating children the following doses are given

Age	Dose per injection ml	Total dose for course ml
Up to 6 months old	0.1–0.3	2–3.2
From 6 months to 1 year	0.1–0.3	4
1–3 years	0.2–0.4	4–4.8
3–5 "	0.4–0.6	6–8
5–10 "	0.6–0.8	8–10
10–15 "	0.7–0.8	10–12

Injections are given twice a week Before each administration the vial containing the preparation must be thoroughly shaken In order to obtain a homogeneous emulsion more quickly it is advisable to warm the vial in warm water

Precautionary measures possible complications and contraindications are the same as when biochinol is used

Available in vials containing 100 ml

To be stored in a cool place protected from light observing safety precautions (List B)

BITHIUROL (Bithiurolum)

11% suspension of the complex compounds of bismuth and thiourea in neutral persic oil 1 ml contains 0.036 g metallic bismuth

Carmine red thick homogeneous liquid On long standing separates forming an upper yellow oil layer and a dense carmine red lower layer

Used for the treatment of all forms of syphilis Injected intramuscularly into the upper outer quadrant of the buttocks Can be used for patients with biochinol intolerance because of heightened sensitivity to quinine

Administered to adults in a dose of 1 ml each second day total dose for the course 24–25 ml

Precautionary measures, possible complications and contraindications are the same as for biochinol and bismoverol

Available in vials containing 100 g

To be stored in a cool dry place observing safety precautions (List B)

PENTABISMOL (Pentabismolum)

Water soluble bismuth preparation 1 ml contains 0.01 g metallic bismuth Aqueous solutions are transparent and colourless and are of neutral reaction

Used for the treatment of all forms of syphilis More quickly absorbed than oil preparations of bismuth Injected intramuscularly in various groups of muscles at a rate of 1 ml in 24 hrs The first day adults are given an injection of 1 ml after an interval of one day 2 ml are injected and then 2 ml each second day Total dose for course for adults 40–50 ml Injections must be given slowly

When using the preparation there may be tenderness at the site of injection to lessen the pain 0.5 ml 2% procaine hydrochloride can be injected simultaneously (in the same syringe) In rare cases patients may develop nephropathy and a "bismuth border"

Contraindications are the same as for other bismuth preparations

Available in ampoules containing 2 ml of aqueous solution

c) Mercury preparations

MERCURIC OINTMENT, GREY (Unguentum hydrargyri cinereum).

Consists of mercury, anhydrous lanolin, purified lard and purified tallow. Contains 30% metallic mercury. Homogeneous grey ointment.

Used topically for rubbing into the skin in the treatment of syphilis (especially in unresponsive cases, and in diseases of the sense organs and the nervous system) and in parasitic skin diseases.

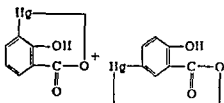
In syphilis, 36—40 applications are prescribed for the course of treatment, the ointment is rubbed in on various parts of the body till the skin is dry (best done before retiring), in order to avoid inflammation of the follicles and intoxication, the ointment should not be applied to the hairy parts of the body. Dose for 1 application for adults 3—5 g.

Contraindications: eczema, ichthyosis, prurigo, amphotomosis, kidney disease, pulmonary tuberculosis.

To be stored in well closed non metallic jars (glass or porcelain) in a cool place.

MERCURIC SALICYLATE (Hydrargyrum salicylicum, Acidum mercuris-salicylicum)

Ortho and para anhydro mercury salicylic acids



White or slightly coloured amorphous powder, odourless and tasteless, almost insoluble in water and alcohol, freely soluble in solutions of sodium hydroxide and sodium carbonate, also soluble, on heating, in sodium chloride solution. Contains approximately 55% mercury.

Used in the treatment of syphilis. Injected intramuscularly in the form of a 10% suspension in olive or persic oil. Before filling the syringe the suspension is warmed in hot water and thoroughly shaken. The injection is made in two steps: the needle is first introduced into the upper outer quadrant of the buttocks and if no blood shows the syringe is then attached and the injection given slowly. If a drop of blood should appear in the needle, showing that it has entered a blood vessel, it is withdrawn and the injection made in another place.

1 ml is administered once in 5 days, the course consists of 10—12 injections. Maximal dose for adults intramuscularly 0.1 g (once in 5 days).

To be kept locked (List A) in well stoppered bottles of amber glass.

MERCURIC CYANIDE (Hydrargyrum cyanatum, Hydrargyri cyanidum)

$\text{Hg}(\text{CN})_2$. Colourless transparent crystals, freely soluble in water (1:13 in cold water and 1:3 in boiling water), soluble in alcohol (1:12). Contains 79% mercury.

Used for the treatment of syphilis and also as a disinfectant.

Administered intramuscularly or intravenously in the treatment of syphilis. Intramuscularly, 1 ml 2% solution is injected once in 2 days. The course of treatment consists of 20 injections. Intravenously, a 1% solution is used, beginning with a dose of 0.5 ml and subsequently increasing the dose to 0.75 and 1 ml. Administered daily for 30—40 days. Intravenous administration is chiefly indicated when it is necessary quickly to influence the process (syphilis of the nervous system, mouth, larynx, etc.).

Maximal doses for adults, intramuscularly, single and daily — 0.02 g. Intravenously — 0.01 g.

Used as a disinfectant for washing and irrigation in inflammatory processes in the form of 1:1000 and 1:2000 solutions

To be kept locked (List V) in glass bottles with ground glass stoppers

MERCURIC BINIODIDE, Mercuric iodide red (*Hydrargyrum binodatum* *Hydrargyri iodidum rubrum*) HgI_2

Fine bright red powder odourless very sparingly soluble in water freely soluble in potassium iodide solution sparingly soluble in alcohol Contains 44% mercury

Used in the treatment of syphilis (tertiary period in affections of the internal organs)

Administered orally in the form of a mixture containing potassium iodide in a dose of 0.005–0.01 g 2–3 times a day

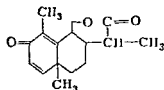
Maximal doses for adults single—0.02 g daily—0.06 g

To be kept locked (List A) in well stoppered bottles of amber glass in a place protected from light

F Anthelmintics

- a) *Drugs chiefly used for the treatment of intestinal nematodiasis* (ascariasis ankylostomiasis enterobiasis trichocephaliasis strongyloidiasis etc)

SANTONIN (*Santoninum*)



Synonym Santolactone

Colourless crystalline powder becoming yellow on exposure to light odourless bitter taste very sparingly soluble in water (1:250 in boiling water) sparingly soluble in alcohol (1:45) Melting point 171–174° Obtained from Levant wormseed (*Artemisia Cina Berg*) family Compositae, which grows mainly in Central Asia

Used for the treatment of ascariasis

The drug is given in tablets or powders 3 times a day for 2 days in succession according to one of the following methods

First method (recommended for adults and for children over 3 years old) 1st day—diet laxative on retiring 2nd day—santonin given on an empty stomach 1 tablet or 1 powder every hour 3 doses in all a laxative is given 1 hr after the 3rd dose (magnesium sulphate or sodium sulphate) and a light breakfast 1 hr after the laxative This procedure is repeated on the following days

Second method (recommended for children up to 3 years old and for weak patients) 1st day—diet laxative on retiring 2nd and 3rd day—1 tablet or 1 powder of santonin 3 times a day 1½–2 hrs before meals after last dose of santonin laxative before retiring

Santonin is administered in the following doses adults—0.08–0.1 g children—0.005 g for each year of their age

Maximal doses for adults single—0.1 g daily—0.4 g

Maximal doses for children from 6 months to 1 year single—0.005 daily—0.015 g 2 years single—0.01 g daily—0.03 g 3–4 years single—0.015–0.02 g daily—0.045–0.06 g 5–6 years single—0.03–0.04 g daily—0.09–0.12 g 7–9 years single—0.035–0.045 g daily—0.14 g 10–14 years single—0.05–0.07 g daily—0.15–0.22 g Infants up to 6 months are not prescribed santonin

Laxatives are given in the following doses when using santonin

Patient's age	Magnesium sulphate, g	Sodium sulphate, g	Compound senna infusion ml
2-3 years	—	—	10
4-5 "	10	8	15
6-7 "	12	10	20
8-9 "	14	12	30
10-12 "	20	15	35
13-16 "	2	20	15
17 years and older	30	2	10

Rhubarb (powder) is given simultaneously with santonin the dose being 10 times that of santonin. On the 2nd day of treatment a salt laxative is given 1 1/2 hrs after the second powder of santonin and rhubarb.

Phenolphthalein and isaphenine are given simultaneously with the 3rd powder of santonin the dose for adults is 1-2 tablets that for children — 1/2-1 tablet.

Compound licorice powder is given to children once a day for 2 days immediately after the last dose of santonin children from 2-3 years old — 1/2 teaspoonful 4-6 years — 1 teaspoonful 8-16 years — 1 1/4-3 teaspoonfuls 17 years and older — 1 teaspoonful.

The day before treatment with santonin the days of treatment and the following day nutritious easily digested liquid food with little fat is prescribed soup thin porridge meat and vegetables rubbed through a sieve milk, sour milk etc.

Santonin is contraindicated in nephrosis nephritis acute gastrointestinal and febrile diseases (not associated with ascariasis). In the case of pregnant women and nursing mothers it is recommended that treatment should be carried out with patients confined to their beds and that the second method should be used (santonin 3 times a day) along with mild laxatives (phenolphthalein or rhubarb) and enemas.

Overdosage of santonin causes vomiting diarrhea respiratory and cardiac depression xanthopsia and convulsions. When taken in the usual doses the urine becomes yellow or orange coloured.

Available in powder form and in tablets of 0.01 0.02 0.04 and 0.05 g. To be stored in well stoppered bottles of amber glass in a place protected from light observing safety precautions (List B).

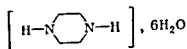
SANTONICA LEVANT WORMSEED (Flos Cinae)
Dried unexpanded flower heads of *Artemisia Cina Berg*. Contains at least 2% santonin.

Used as an anthelmintic against ascarides. The flower heads are ground in a mortar and given with preserves sugar honey of treacle.

Treatment is according to the second method recommended for santonin.

Age	Dose g
1-3 years	0.25-0.75
4-6 "	1-1.5
7-9 "	1.75-2.25
10-14 "	2.5-3.5
15 "	4
Adults	5

PIPERAZINE (Piperazinum)
Diethylenediamine



Synonyms Eraverm, Multifuge, Oxypip, Parazine Uricid Lvilon, Vermoxyl

Piperazine hexahydrate: colourless crystalline substance deliquescent, soluble in water and alcohol Aqueous solutions are alkaline Melting point 44°

It has been established in recent years that piperazine and its salts have a marked anthelmintic action against various species of nematodes, being especially indicated in ascariasis and enterobiasis Piperazine preparations are more effective than other antiascariasis agents They act on both sexually mature and sexually immature individuals of both sexes

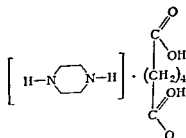
When piperazine preparations are used, the organism is freed from parasites in 90—95% of the cases, by repeating treatment almost 100% dehelminthization can be attained

No preliminary preparation of patients or special diet is required when piperazine is administered Laxatives are given after the course of treatment if evacuation of feces is arrested

Piperazine preparations are only slightly toxic, and when given in therapeutic doses there are usually no side effects they can be used on an out patient basis

Besides piperazine base, the adipinate, sulphate citrate and phosphate are used

Piperazine adipinate (Piperazinum adipicum)

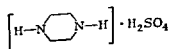


Synonyms Adipalit, Adipazina, Entacyl, Entazin, Helmirazin, Heltolan Nometan, Oxurazin, Piperasat, Vermicomprehn, Vermitox

White crystalline substance, odourless, pleasant weakly acid taste, sparingly soluble in cold water, more readily soluble in hot, sparingly soluble in mineral acids, alcohol and ether Melting point $256-257^\circ$

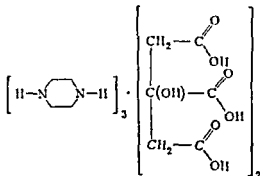
Not hygroscopic, stable on exposure to air

Piperazine sulphate (Piperazinum sulfate)

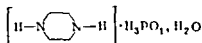


White crystalline substance bitter acid taste, freely soluble in dilute alkalis, insoluble in alcohol and ether Not hygroscopic, stable on exposure to air

Piperazine citrate (Piperazinum citricum)



Synonyms Antepar citrate Citrazine, Helmezine, Multifuge citrate, Oxyzine, Parazine citrate Pipizan citrate Piperazate Santoban, Tasnon, Toxocan
Colourless crystalline substance pleasant weakly acid taste, freely soluble in water Melting point 203–205° Not hygroscopic, stable on exposure to air
Piperazine phosphate (Piperazinum phosphoricum)



Synonyms Antepar Fosfovermin Piperazate

White crystalline substance sparingly soluble in water, freely soluble in solutions of acids and alkalis Not hygroscopic, stable on exposure to air

The salts of piperazine are more convenient to use than the base, since the latter is hygroscopic it can only be used in the form of solutions Piperazine hexahydrate is unstable, and moreover has an unpleasant taste For these reasons it is mostly the salts of piperazine that are used today

All piperazine preparations are administered orally They are used for both adults and children

Doses and length of treatment are the same for all preparations Piperazine salts (adipate sulphate citrate and phosphate) are given in the form of tablets or powders piperazine hexahydrate is given in the form of a 3% solution in sugar syrup (1 tablespoonful contains about 0.5 g piperazine)

In ascariasis piperazine and its salts are administered 2 days in succession Adults are given doses of 1 g 3–4 times a day children are given the following doses

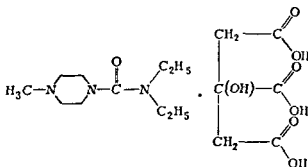
Age	Single dose, g	Number of doses per day
1 year	0.2	2
2–3 years	0.3	2
4–6 "	0.5	2
7–9 "	0.5	3
10–14 "	1	2
15 years and older	1	3–4

The drugs are taken $\frac{1}{2}$ —1 hr after meals. A laxative is given at the end of treatment if there is constipation (phenolphthalein, rhubarb or a salt laxative). A special diet is not necessary during treatment.

In enterobiasis the drugs are administered in the same doses in cycles of 3—5 days with a week's interval between cycles. 2—3 cycles of treatment are carried out, a hygienic regimen must be strictly adhered to.

DITRAZINE (Ditrazinum)

1 Diethylcarbamy 2 methylpiperazine citrate



Synonyms Banacid, Carbamazine, Carbilazin, Caricid, Diaethylcarbamazini citras, Diaethylcarbamazinum, Hetrazan, Notezine, Supatonin.

White crystalline powder, soluble in water and alcohol, insoluble in benzene and ether. Melting point 137—139°.

Used in the treatment of ascariasis and filariasis, especially the latter, less effective in ascariasis than piperazine and its salts.

In the treatment of ascariasis administered orally, 0.2 g 3 times a day for 2—3 days in succession. A laxative is given in the evening on the days ditrazine is taken. In filariasis (wucheriasis, loasis) ditrazine is administered in a dose of 0.002 g per kg body weight, 3 times a day for 2—3 weeks.

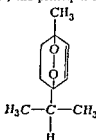
CHENOPODIUM OIL (Oleum Chenopodii)

Volatile oil contained in American wormseed (*Chenopodium anthelminticum* L.), Goosefoot family (*Chenopodiaceae*).

Synonym Aetheroleum Chenopodii.

Pale yellow oil, becoming brown on exposure to air, sharp, characteristic odour reminiscent of turpentine, bitter, burning taste. Sp. gr. — 0.965—0.990 at 15°.

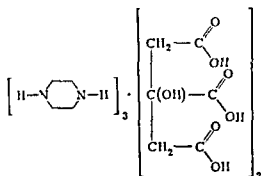
Soluble in alcohol. Contains 60—80% ascaridol, the principal active constituent.



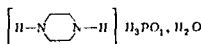
Ascaridol

Chenopodium oil is used for the treatment of ascariasis and ankylostomiasis. It is very effective in ascariasis but must be used with caution because of the high toxicity.

Piperazine citrate (Piperazinum citricum)



Synonyms Antepar citrate Citrazine Helmcizine Multifuge citrate Oxyzine Parazine citrate Pipizan citrate Piperazate Santoban Tasnon Toxocan
 Colourless crystalline substance pleasant weakly acid taste freely soluble in water Melting point 203—205° Not hygroscopic stable on exposure to air
 Piperazine phosphate (Piperazinum phosphoricum)



Synonyms Antepar Foslovermin Piperazate

White crystalline substance sparingly soluble in water freely soluble in solutions of acids and alkalis Not hygroscopic stable on exposure to air

The salts of piperazine are more convenient to use than the base since the latter is hygroscopic it can only be used in the form of solutions Piperazine hexahydrate is unstable and moreover has an unpleasant taste For these reasons it is mostly the salts of piperazine that are used today

All piperazine preparations are administered orally They are used for both adults and children

Doses and length of treatment are the same for all preparations Piperazine salts (adipate sulphate citrate and phosphate) are given in the form of tablets or powders piperazine hexahydrate is given in the form of a 3% solution in sugar syrup (1 tablespoonful contains about 0.5 g piperazine)

In ascariasis piperazine and its salts are administered 2 days in succession Adults are given doses of 1 g 3—4 times a day children are given the following doses

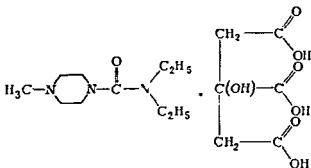
Age	Single dose g	Number of doses per day
1 year	0.2	2
1—3 years	0.3	2
4—6 "	0.5	2
7—9 "	0.5	3
10—14 "	1	2
15 years and older	1	3—4

The drugs are taken $\frac{1}{2}$ —1 hr after meals. A laxative is given at the end of treatment if there is constipation (phenolphthalein, rhubarb or a salt laxative). A special diet is not necessary during treatment.

In enterobiasis the drugs are administered in the same doses in cycles of 3—5 days with a week's interval between cycles. 2—3 cycles of treatment are carried out. A hygienic regimen must be strictly adhered to.

DITRAZINE (Ditrazinum)

1 Diethylcarbamyl 2 methylpiperazine citrate



Synonyms: Banocid, Carbamazine, Carbilazin, Caricid, Diaethylcarbamazini, citras, Diaethylcarbamazinum, Hetrazan, Notezine, Supatonin.

White crystalline powder, soluble in water and alcohol, insoluble in benzene and ether. Melting point 137—139°.

Used in the treatment of ascariasis and filariasis, especially the latter, less effective in ascariasis than piperazine and its salts.

In the treatment of ascariasis administered orally 0.2 g 3 times a day for 2—3 days in succession. A laxative is given in the evening on the days ditrazine is taken. In filariasis (wucheriasis loasis) ditrazine is administered in a dose of 0.002 g per kg body weight 3 times a day for 2—3 weeks.

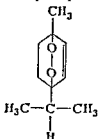
CHENOPODIUM OIL (Oleum Chenopodii)

Volatile oil contained in American wormseed (*Chenopodium anthelminticum* L.), Goosefoot family (Chenopodiaceae).

Synonym: Aetheroleum Chenopodii.

Pale yellow oil becoming brown on exposure to air, sharp characteristic odour reminiscent of turpentine, bitter burning taste. Sp. gr. — 0.965—0.990 at 15°.

Soluble in alcohol. Contains 60—80% ascaridol, the principal active constituent.



Ascaridol

Chenopodium oil is used for the treatment of ascariasis and ankylostomiasis. It is very effective in ascariasis but must be used with caution because of the high toxicity.

Chenopodium oil irritates the mucous membranes and causes intensified salivation and excretion of gastric juice. In large doses causes stimulation of the central nervous system followed by depression and paralysis, has a depressing effect on the cardiovascular system and may cause changes in the kidneys and liver.

The absorption and toxicity of *chenopodium* oil are somewhat reduced when laxatives, particularly castor oil, are given simultaneously.

Treatment is carried out in hospital or day clinic. On the day of treatment and for 2 days before and after treatment, fats and alcoholic beverages should be excluded from the diet and patients should be prescribed light food, rich in carbohydrates. An enema is given in the evening before the day of treatment. Laxatives are contraindicated before treatment. On the day of treatment the patient receives a light breakfast: a cup of tea with sugar and 100 g bread. 2 hrs after breakfast the patient is given a dose of *chenopodium* oil (see below) with castor oil (40 g for adults) or with 30% magnesium sulphate or sodium sulphate solution (100–150 ml for adults). For children the dose of laxative depends on the age.

Age	Dose of <i>chenopodium</i> oil, ml
2–3 years	0.1–0.2
4–5 "	0.3
6–8 "	0.4
9–10 "	0.6
11–12 "	0.8
13–16 "	1
17 years and older	1–1.5

In ankylostomiasis the dose for adults can be increased to 2 ml.

Maximal dose for adults 2 ml (single administration).

Chenopodium oil is measured out with a graduated pipette, mixed with the laxative (preferably castor oil) and given to the patient in a single administration. Breakfast is permitted 3–4 hrs afterwards. If evacuation of feces should be arrested, an enema or additional laxative is given. The evacuation of parasites usually begins the first day and continues 3 days.

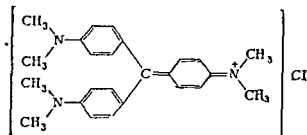
Contraindications: diseases of liver and kidneys, ulcer and acute diseases of gastrointestinal tract, pregnancy, organic diseases of the nervous system (epilepsy, encephalitis, poliomyelitis, etc.). *Chenopodium* oil must not be given in acute febrile diseases and must not be administered to emaciated patients or the aged.

Possible complications: nausea, vomiting, pains in the stomach, weak, retarded pulse. The administration of larger doses may cause loss of consciousness, convulsions, shallow respiration and impairment of vision and hearing. If complications should develop, stomach lavage is performed and cardiants administered.

Treatment with *chenopodium* oil (in the presence of indications) must not be repeated sooner than in 1–2 months and only after the patient has been thoroughly examined.

To be stored in well stoppered bottles in a cool place, observing safety precautions (List B).

GENTIAN VIOLET (Gentianvioletum).
Hexamethylpararosanine chloride



Synonyms Crystal violet, Hexamethyl violet, Methylrosanilini Chloridum; Methyl violet, Vianin

Dark violet crystalline powder, soluble in water, alcohol, and glycerol, insoluble in ether

Administered orally as an anthelmintic in enterobiasis and strongyloidiasis. Applied locally as an antiseptic in pyoderma, sycosis and other skin diseases

In the treatment of enterobiasis, gentian violet is administered in three 5 day cycles with intervals of 7 days between. Adults are given doses of 0.08—0.1 g 3 times a day, children are given 0.005 g for each year of their age twice a day. Administered in capsules or pills an hr before meals (small children are given the drug in a powder mixed with sugar)

In the treatment of strongyloidiasis, the drug is administered in the same doses 15 days in succession, if necessary a second course of treatment (7—10 days) is given in 1—2 months

Patients taking gentian violet complain at times of nausea, pains in the stomach and headache, vomiting sometimes occurs. When the drug is tolerated badly it is given an hr after meals, dilute hydrochloric acid and ethyl aminobenzoate are prescribed during meals

During treatment patients must refrain from fat food and alcoholic beverages

Gentian violet is excreted in the feces and urine, imparting a pink violet colour to them

0.5, 1 and 2% solutions and ointments are used for external application

Oral administration contraindicated in diseases of the kidneys and liver

b) Drugs chiefly used for the treatment of intestinal cestodiasis (teniasis, hymenolepiasis, diphylobothriasis)

MALE FERN, ETHEREAL EXTRACT (Extractum Filicis maris aethereum).

Obtained from the dried rhizome of the Male Fern—*Dryopteris filix mas* (L.) Schott, a true fern of the family Polypodiaceae

Thick, unmobile mass of green or brownish green colour, disagreeable, "scratchy" taste, insoluble in water, freely soluble in alcohol and ether

The chief active principles of the extract are filix acid and filmaron—derivatives of filicic acid

Acts mainly against tapeworms

Used in the treatment of teniasis (infestation with ox and swine tapeworms), diphylobothriasis (infestation with the broad tapeworm) and hymenolepiasis (infestation with the dwarf tapeworm). Also used for the treatment of enterobiasis

In the treatment of teniasis, the extract is given for one day. The urine must be analyzed before dehelminthization 1—2 days before treatment. nutritious, easily assimilated food containing little fat is prescribed: white bread, dry toast, groat soups, milk, sour milk, curds, thin milk porridge, boiled fresh fish, jelly, coffee, tea. Sugar is permitted.

On the eve of treatment supper is replaced by a cup of sweet tea or coffee with dry toast and a laxative is given before retiring

Adults and children over 5 years old are given magnesium sulphate sodium sulphate or compound senna infusion children under 5 years old are given compound senna infusion or phenolphthalein Castor oil must not be given

An enema is given in the morning on the day of treatment after which capsules containing fern extract are given for 30 min (to be drunk down with water)

Patient's age	Dose of fern extract g
2 years	1
3	1.5
4	2
5-6	2-2.5
7-9	3-3.5
10-17	3.5-4
17-50 "	4-7

If capsules are not available and also in the case of small children fern extract is given with honey preserves or sugar in two half doses with an interval of 15-20 min between Male fern can be administered in the form of an emulsion (for example 3 g male fern 0.5 g sodium bicarbonate and 30 ml peppermint water) or freshly prepared boluses 1 part fern extract is mixed with 1 part finely powdered rose hips and $\frac{1}{2}$ part 50% glycerol added after mixing $\frac{1}{2}$ - $\frac{3}{4}$ part powdered rose hips is added

A salt laxative is given 30 min after the last dose of extract In $1\frac{1}{2}$ -2 hrs the patient is given a light breakfast If there is no evacuation in 3 hrs after the administration of the laxative a warm enema is given If the parasite is evacuated without the head 1-3 more enemas are given

It has been reported that fern extract is sufficiently effective when used in smaller doses 3-4 g for adults and correspondingly less for children (N Y Semyonova)

Treatment of hymenolepiasis is carried out in 3 cycles with intervals of 10-12 days Each cycle consists of 2 days of preparation and 1 day of treatment 1st day - diet nutritious easily assimilated food contained little fat 2nd day - diet laxative in the evening 3rd day - enema in the morning followed in 20 min by administration of fern extract on empty stomach Adults are usually given doses of 2.5-3 g Doses for children 2 years old - 0.3 g 3-4 years - 0.6 g 5-6 years - 0.9 g 7-8 years - 1.2 g 9-10 years - 1.5 g 11-12 years - 1.8 g 13-14 years - 2.2 g 15-16-17 years and older - 2.5-3 g It has been reported that smaller doses are sufficiently effective 1-1.5 g for adults children from 1 year to 2 years - 0.2 g 3-4 years - 0.3 g 5-6 years - 0.5 g 7-8 years - 0.6 g 9-10 years - 0.7 g 11-12 years - 0.9 g 13-16 years - 1 g The course of treatment also consists of 3 cycles with 10-12 day intervals (M Y Turchins and N Y Semyonova)

In diphyllorhynchiasis (infestation with the broad tapeworm) treatment is carried out in the same way as in teniasis

In enterobiasis fern extract is administered in the same way as in the treatment of hymenolepiasis but without the third cycle

Maximal dose of male fern extract for adults - 8 g (in a single administration)

Maximal doses for children (single administration) 2 years old - 1 g 3-4 years - 1.5-2 g 5-6 years - 2.5-3 g 7-9 years - 3.5-4 g 10-14 years - 5 g Not prescribed for infants up to 2 years old

Side effects may occur when male fern extract is used Because of the irritating effect on the mucous membrane of the gastrointestinal tract the preparation may cause nausea vomiting and diarrhea in rare cases the stools may be bloody In pregnant women there may be abortion as a consequence of the reflex contraction of the uterine muscles On being absorbed from the gastrointestinal tract the preparation may cause changes involving the nervous system (vertigo and

headache, and in rare cases convulsions, depression of respiration and atrophy of the optic nerve), the cardiovascular system (weakening of cardiac activity and collapse), and the liver (degenerative changes). Treatment with male fern extract should be carried out under the careful observation of a physician.

Contraindications decompensated heart disease, diseases of the liver and kidneys, ulcer of the stomach and duodenum, acute gastrointestinal and febrile diseases, pregnancy, acute emaciation, anemia, active tuberculosis.

Safety precautions are to be observed during storage. Extract that has turned brown is unfit for use.

FILIXAN (Filixanum).

Dry extract of male fern. Yellowish brown amorphous powder, odourless and almost tasteless. Insoluble in water, soluble in alkalis.

Available in tablets of 0.5 g.

In teniasis, administered in a single dose of 14–16 tablets for adults (7–8 g). Dose for children: 2–5 years old — 2–5 tablets (1–2.5 g); 6–10 years — 6–8 tablets (3–4 g); 11–15 years — 10–12 tablets (5–6 g).

Maximal dose for adults — 20 tablets (10 g).

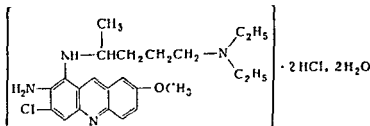
Preparation of patients and method of treatment are the same as for ethereal extract of male fern.

Possible complications and contraindications are also the same.

To be stored in well stoppered bottles in a place protected from light, observing safety precautions (List B).

AMINOACRICHIN (Aminoacrichinum)

2-Methoxy-6-chloro-7-amino-9- δ -diethylamino- α -methylbutylaminoacridine dihydrochloride.



Orange yellow powder, freely soluble in water. Melting point 260–262°.

In chemotherapeutic properties aminoacrichin is similar to quinacrine. It has an antimalarial action and is effective in the treatment of some cestodiasis also used in the treatment of trichomonadal colpitis. Used in veterinary practice for the treatment of theileriasis in cattle.

Aminoacrichin is less toxic than quinacrine.

In hymenolepiasis aminoacrichin is mostly used when male fern preparations are contraindicated. In stubborn cases of hymenolepiasis, aminoacrichin can be given during the intervals between administrations of fern extract. Administered orally once a day in the morning on an empty stomach, adults are given 0.3–0.4 g, 6-year-old children — 0.15 g, 8 years — 0.2 g; 13–15 years — 0.3 g. The course of treatment consists of 3–4 cycles each of 3 days with intervals of 5–6 days. A laxative is given on the eve of treatment and on the day of treatment (in 1/2–1 hr after the administration of aminoacrichin).

In the treatment of trichomonadal colpitis, aminoacrichin is applied locally and administered orally simultaneously. Locally 0.05–0.1 g is used, orally — 0.1 g 3 times a day.

Locally 1/2 tablet (0.05 g of the drug) is introduced into the cervical canal with an ear forceps. Applied every 3–4 days, total number of applications — 3–4. In cases where introduction into the cervical canal is impossible, aminoacri-

chin is used in the form of a 2% paste 5 g of paste is applied once in 3 days, a total of 8 applications. If the patient is unable to go to the physician regularly, the drug is prescribed in globules containing 0.05 g, which are introduced before retiring once in 2—3 days, 3—4 times in all. In the intervals, globules that do not contain aminoacrichin are used.

The course of local treatment is repeated over a period of 3 ovarian cycles immediately after the end of menstruation.

Orally, aminoacrichin is administered in a dose of 0.1 g daily 3 times a day for 5 days simultaneously with the first course of local treatment or at the end of the course. The drug is not prescribed orally when the course of local treatment is repeated.

When aminoacrichin is applied locally symptoms of irritation may be observed: desquamation of the epithelium, ichorous discharge, edema of the genitals. There may also be a transitory elevation of the temperature. If side effects should arise treatment is temporarily discontinued after which pathological symptoms pass away of themselves.

Local application of aminoacrichin is contraindicated in senile sclerotic changes in the vaginal mucosa. The drug should not be administered intracervically during pregnancy. Orally, the drug is not prescribed in gastritis and ulcer of the stomach and duodenum.

Available in powder form and in tablets of 0.1 and 0.3 g.

To be stored in well stoppered glass bottles, observing safety precautions (List B).

POMEGRANATE BARK (*Cortex Granati*).

Dried bark of the trunk, branches and roots of the pomegranate tree (*Punica granatum* L.), family Punicaceae, which grows in the southern regions of the USSR.

Contains alkaloids among them pelletierine, isopelletierine and methylisopelletierine as well as tannin resin, starch and other substances.

Extract and infusions of pomegranate bark are used in medicine in infestations with various species of tapeworms (with the exception of the dwarf tapeworm). Since pomegranate preparations are less effective than male fern preparations they are only used in cases where treatment with male fern is contraindicated. Pomegranate infusion is prepared in the following way: 40—50 g finely divided bark is soaked for 6 hrs in 400 ml water and then boiled down to 200 ml, strained and cooled. After the usual preparation the patient is given the designated amount to drink in one hr. A salt laxative is given in half an hour. Aqueous and acetic acid extracts are also used.

Pomegranate bark preparations must be used with caution because of the possibility of side effects: vertigo, general weakness, convulsions and impairment of vision.

c) Drugs chiefly used for the treatment of extraintestinal helminthiasis

HEXACHLOROETHANE (Fasciolin) (*Hexachloroethanum*) $\text{CCl}_3-\text{CCl}_3$

White crystalline powder, characteristic odour reminiscent of camphor, almost insoluble in water, soluble in ether and fats.

Used for the treatment of opisthorchiasis and fascioliasis.

Administered orally in gelatine capsules. On the first and second day of treatment, an hour after a light breakfast, the patient takes 1 g of the drug every 10—15 min, a total of 6—8 g. The course of treatment is for 2 days, total dose 12—16 g.

Side effects may occur when hexachloroethane is used: vertigo, feeling of intoxication, general weakness, and pain in the region of the heart.

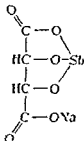
Contraindicated in diseases of the liver and kidneys with impairment of their function, and in cardiovascular insufficiency. Treatment should be carried out under the careful observation of a physician.

Available in powder form.

To be stored in bottles with ground glass stoppers

Note Hexachloroethane is not to be confused with Hexachloran, which is an insecticide and has toxic properties

SODIUM ANTIMONYL TARTRATE (Natrium tartarico-stibicum)



White crystalline powder, soluble in water

Has a chemotherapeutic action against trematodes

Used in the treatment of schistosomiasis opisthorchiasis, and clonorchiasis

Administered intravenously in the form of a 1% solution in isotonic saline with the addition of 5% glucose. The solution should be freshly prepared and sterilized in the autoclave or on a water bath. To be injected slowly (not faster than 2 ml per min). Treatment should only be carried out on an inpatient basis.

The course of treatment usually consists of 20 daily injections. The dose per injection is 1–12 mg per kg body weight. The total dose for the course should not exceed 13 g (130 ml 1% solution). In order to avoid side effects the dose is lowered somewhat after 10–11 injections and again increased beginning with the 15th injection. For example, a patient weighing 60 kg is given an injection of 5 ml 1% solution of the first time, 7 ml from the 2nd to the 11th injection, 5 ml from the 12th to the 15th injection and 7 ml from the 16th to the 20th injection, in all 130 ml. In opisthorchiasis and clonorchiasis intensive treatment is more effective. 3 ml 1% solution is injected intravenously 2–3 days before beginning the basic course of treatment. If tolerance is good a 3 day course of treatment is carried out, 2 injections a day with an interval of 3 hrs between, a total of 6 injections. The single dose is 1.5–2 mg per kg body weight, the daily dose — 3–4 mg per kg body weight so as to give a total dose of 10 mg per kg body weight for the course. (A patient weighing 60 kg is given 60 ml 1% solution during the 3 days).

Side effects may occur when using the drug: nausea, vomiting, loss of appetite, headache, elevated temperature, lowering of arterial pressure, etc.

Contraindicated in organic heart disease, diseases of the liver and kidneys (not associated with helminthiasis), pregnancy, menstruation, emaciation and senility.

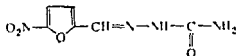
G. Miscellaneous chemotherapeutic drugs

a) Nitrofurans

Recent investigations have shown that many derivatives of 5 nitrofurans have pronounced antibacterial activity. Compounds of this series act on gram positive and gram negative microbes, as well as on large viruses and some protozoa. In some cases they inhibit the growth of microorganisms that have become resistant to sulfanilamides and antibiotics.

Two drugs of this group — nitrofurazone and nitrofurantoin — have found application today in medical practice.

NITROFURAZONE (Nitrofurazonum) 5 Nitro 2 furfurylidene semicarbazone



Synonyms Furacilin Furacin Furalon Furosem Nitrofurazone Vabrocid Vitrocin

Yellow fine crystalline powder faint bitter taste very slightly soluble in water (1:4200) sparingly soluble in alcohol practically insoluble in ether soluble in alkalis Melting point 227—232°

Nitrofurazone is an antibacterial substance which acts on various gram positive and gram negative microbes (staphylococci streptococci dysentery bacilli coli bacilli paratyphoid bacilli the causative organism of gas gangrene etc.) Used topically for the prevention and treatment of purulent inflammatory processes and orally for the treatment of bacillary dysentery

Solutions of nitrofurazone do not irritate the tissues but promote the granulation and healing of wounds The drug is effective in anaerobic infections

Nitrofurazone is used in treating unhealing wounds osteomyelitis wounds of the joints empyema and phlegmons purulent dermatitis also used in otorhinolaryngological ophthalmological dermatological and stomatological practice

Indications and methods of use a) in suppurating wounds bedsores and ulcers and II and III degree burns and in preparing granulating surfaces for skin grafting and for a second suture—the wound is irrigated with an aqueous solution and a moist dressing applied b) in amputations—the stump is irrigated with an aqueous solution and covered with a moist dressing c) in osteomyelitis—after the operation the cavity is irrigated with an aqueous solution and a moist dressing applied d) in wounds of the joints—the wound is treated as described above and 20—25 ml of solution is instilled into the cavity of the joint e) in pleural empyema—the pus is aspirated and the cavity irrigated after which 20—100 ml of solution is instilled f) in anaerobic infections—besides the usual surgical intervention the wound is treated with nitrofurazone g) in otorhinolaryngological practice—alcoholic solution used in the form of drops in chronic suppurative otitis likewise used in furuncles of the auditory canal and chronic empyema of the accessory sinuses of the nose for irrigating the antrum of Highmore and the accessory sinuses of the nose an aqueous solution of nitrofurazone is used h) in ophthalmological practice—in conjunctivitis and scrofulous diseases of the eye an aqueous solution is instilled into the conjunctival sac in blepharitis nitrofurazone ointment is applied to the margins of the lids

Nitrofurazone is used in the enumerated indications in the following forms 1) 1:5000 aqueous solution 2) 1:1500 alcoholic solution and 3) 1:500 ointment

The aqueous solution is prepared by dissolving 1 part nitrofurazone in 5000 parts isotonic saline or distilled water For more rapid solution the use of boiling or hot water is to be recommended after which the solution is cooled to room temperature Aqueous solutions can be used for lengthy periods but inasmuch as nitrofurazone does not possess fungicidal properties solutions must be protected from fungal infection Aqueous solutions are sterilized in the usual way

The alcoholic solution is prepared by dissolving 1 part nitrofurazone in 1500 parts 70° alcohol The alcoholic solution can be kept for an unlimited period of time

Nitrofurazone ointment is prepared by first dissolving the drug in a small amount of liquid petrolatum (best let stand for 10—20 hrs) and then adding the necessary amount of castor oil fish liver oil and lanolin Oil solutions and ointments can be kept for an unlimited time

In the treatment of acute bacillary dysentery nitrofurazone is administered orally in a dose of 0.1 g 4 times a day for 5—6 days (for adults) After a four

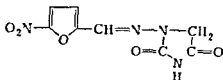
day break the course of treatment is repeated giving the drug in the same dose (0.1 g) 4 times a day for 4 days

Available in powder form and in tablets of 0.1 g

To be stored in well stoppered bottles of dark glass in a cool place protected from light observing safety precautions (List B) The powder and solutions may turn brown on standing but their potency remains unchanged

NITROFURANTOIN (Nitrofurantoinum)

N (5 Nitro 2 furfurylidene) 1 aminohydantoin



Synonyms Chemisufuran Furadantin Furadonine Furazidin Furina Nifurantin

Yellow fine crystalline powder bitter taste very sparingly soluble in water (1:8000) and alcohol (1:2000) Melting point 258–263° (with decomposition)

Nitrofurantoin is a potent antimicrobial agent acts on gram positive and gram negative microbes (staphylococci streptococci coli bacilli the causative agents of typhoid fever paratyphoid and dysentery and various strains of *Proteus*)

Extremely effective in the treatment of infectious diseases of the urinary tract Indicated for the therapy of pyelitis pyelonephritis cystitis and urethritis Also used for the prevention of urological infections in urological operations cystoscopy catheterization etc

Administered orally in a daily dose of 5–8 mg per kg body weight Adults are usually given 0.1–0.15 g 3–4 times a day Course of treatment 5–8 days If there is no effect within this period further treatment is of no advantage

The use of nitrofurantoin may in some cases cause loss of appetite nausea heart burn and at times vomiting Exanthema and enanthema of an allergic character are likewise possible

In order to avoid these manifestations the drug is best taken on an empty stomach and drunk down with sufficient liquid If side effects should arise the dose of nitrofurantoin must be reduced and dimedrol calcium chloride vitamins PP and B₁ and glucose administered

If there should be pronounced side effects administration of nitrofurantoin should be discontinued

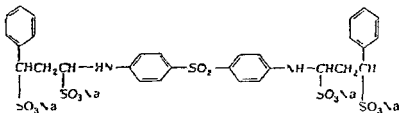
Available in powder form and in tablets of 0.05 and 0.1 g

To be stored in dark containers in a place protected from light observing safety precautions (List B)

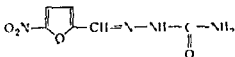
b) Sulfones

SOLUSULFONE (Solusulfonum)

Tetrasodium salt of 4,4-bis (3-phenyl-1,3-disulfo-propylamino) diphenylsulfone



NITROFURAZONE (Nitrofurazonum)
5 Nitro 2 furfurylidene semicarbazone



Synonyms Furacilin Furacin Furalon Furosem Nitrofurazone Vabron Vitrocin

Yellow fine crystalline powder faint bitter taste very slightly soluble in water (1:4200) sparingly soluble in alcohol practically insoluble in ether, soluble in alkalis Melting point 227—232°

Nitrofurazone is an antibacterial substance which acts on various gram positive and gram negative microbes (staphylococci streptococci dysenteriae coli bacilli paratyphoid bacilli the causative organism of gas gangrene etc.) Used topically for the prevention and treatment of purulent inflammatory processes and orally for the treatment of bacillary dysentery

Solutions of nitrofurazone do not irritate the tissues but promote the granulation and healing of wounds The drug is effective in anaerobic infections

Nitrofurazone is used in treating unhealing wounds osteomyelitis wounds of the joints empyema and phlegmons purulent dermatitis also used in otorhinolaryngological ophthalmological dermatological and stomatological practice

Indications and methods of use a) in suppurating wounds bedsores ulcers and II and III degree burns and in preparing granulating surfaces skin grafting and for a second suture—the wound is irrigated with an aqueous solution and a moist dressing applied b) in amputations—the stump is irrigated with an aqueous solution and covered with a moist dressing c) in osteomyelitis—after the operation the cavity is irrigated with an aqueous solution and a moist dressing applied d) in wounds of the joints—the wound is treated as described above and 20—25 ml of solution is instilled into the cavity of the joint e) in pleural empyema—the pus is aspirated and the cavity irrigated after which 20—100 ml of solution is instilled f) in anaerobic infections besides the usual surgical intervention the wound is treated with nitrofurazone g) in otorhinolaryngological practice—alcoholic solution used in the form of drops in chronic suppurative otitis likewise used in furuncles of the auditory canal and chronic empyema of the accessory sinuses of the nose for irrigating the antrum of Highmore and the accessory sinuses of the nose an aqueous solution of nitrofurazone is used h) in ophthalmological practice—in conjunctivitis and scrofulous diseases of the eye an aqueous solution is instilled into the conjunctival sac in blepharitis nitrofurazone ointment is applied to the margins of the lids

Nitrofurazone is used in the enumerated indications in the following form 1) 1:5000 aqueous solution 2) 1:1500 alcoholic solution and 3) 1:500 ointment

The aqueous solution is prepared by dissolving 1 part nitrofurazone in 5000 parts isotonic saline or distilled water For more rapid solution the use of boiled or hot water is to be recommended after which the solution is cooled to room temperature Aqueous solutions can be used for lengthy periods but inasmuch as nitrofurazone does not possess fungicidal properties solutions must be protected from fungal infection Aqueous solutions are sterilized in the usual way

The alcoholic solution is prepared by dissolving 1 part nitrofurazone in 1500 parts 70° alcohol The alcoholic solution can be kept for an unlimited period of time

Nitrofurazone ointment is prepared by first dissolving the drug in a small amount of liquid petrolatum (best let stand for 10—20 hrs) and then adding the necessary amount of castor oil fish liver oil and lanolin Oil solutions and ointments can be kept for an unlimited time

In the treatment of acute bacillary dysentery nitrofurazone is administered orally in a dose of 0.1 g 4 times a day for 5—6 days (for adults) After a few

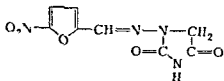
day break the course of treatment is repeated giving the drug in the same dose (0.1 g) 4 times a day for 4 days

Available in powder form and in tablets of 0.1 g

To be stored in well stoppered bottles of dark glass in a cool place protected from light observing safety precautions (List B) The powder and solutions may turn brown on standing but their potency remains unchanged

NITROFURANTOIN (Nitrofurantoinum)

N (5 Nitro 2 furfurylidene) 1 aminohydantoin



Synonyms Chemofuran Furadantin Furadonine Furazidin Furina Nifurantin

Yellow fine crystalline powder bitter taste very sparingly soluble in water (1:8000) and alcohol (1:2000) Melting point 208-263° (with decomposition)

Nitrofurantoin is a potent antimicrobial agent acts on gram positive and gram negative microbes (staphylococci streptococci coli bacilli) the causative agents of typhoid fever paratyphoid and dysentery and various strains of Proteus)

Extremely effective in the treatment of infectious diseases of the urinary tract Indicated for the therapy of pyelitis pyelonephritis cystitis and urethritis Also used for the prevention of urological infections in urological operations cystoscopy catheterization etc

Administered orally in a daily dose of 5-8 mg per kg body weight Adults are usually given 0.1-0.15 g 3-4 times a day Course of treatment 5-8 days If there is no effect within this period further treatment is of no advantage

The use of nitrofurantoin may in some cases cause loss of appetite nausea heart burn and at times vomiting Exanthema and enanthema of an allergic character are likewise possible

In order to avoid these manifestations the drug is best taken on an empty stomach and drunk down with sufficient liquid If side effects should arise the dose of nitrofurantoin must be reduced and dimedrol calcium chloride vitamins PP and B₁ and glucose administered

If there should be pronounced side effects administration of nitrofurantoin should be discontinued

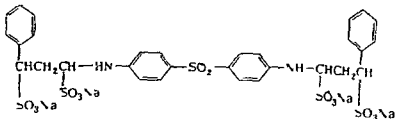
Available in powder form and in tablets of 0.03 and 0.1 g

To be stored in dark containers in a place protected from light observing safety precautions (List B)

b) Sulfones

SOLUSULFONE (Solusulfonum)

Tetrasodium salt of 4,4-bis (3-phenyl 1,3-disulfo-propylamino) diphenylsulfone



Synonyms Cimedone, Solapson, Solasulfonum, Sulfetron, Sulphonazine

White amorphous powder, soluble in water, insoluble in organic solvents

Used for the treatment of leprosy at specialized medical institutions. Administered intramuscularly twice a week in the form of a 50% solution: 1st week — 2 ml per injection, 2nd week — 2.5 ml, 3rd week — 3 ml, and 4th and following weeks — 3.5 ml

In strong subjects the single dose may be increased to 5 ml, while in weak subjects it is reduced. The initial dose is 1 ml, which is increased to 2–2.5 ml. The dose for children is reduced according to their age.

Course of treatment: 6 months followed by a break of 1–1½ months during which general tonic treatment is given.

Solusulfone is also used topically in the form of a 10% solution or ointment in order to accelerate the healing of ulcers.

Side effects may occur during treatment with solusulfone: gastrointestinal disorders, headache, erythematous eruptions, anemia. In order to prevent or overcome anemia, liver preparations, iron and the like are prescribed.

Contraindicated in a florid course of the lepromatous form of leprosy in the L₃ stage with frequent and severe exacerbations, in cases of impairment of the function of liver and kidneys and in cases of impairment of the function of the gastrointestinal tract.

During treatment with solusulfone the administration of aminopyrine and barbiturates is contraindicated.

Available in powder form.

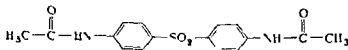
Solutions for injection are prepared in the following way: 50 g solusulfone is dissolved in 60 ml hot distilled water, when completely dissolved, the solution is cooled and distilled water is added to make 100 ml. The solution is thoroughly stirred and filtered through a paper filter.

The filtered solution should be absolutely transparent. It is sterilized in the autoclave for 30 min at a temperature of 115°. Large amounts of solution (more than 500 ml) are sterilized for 45 min. Phenol may be added to large amounts of solution at the rate of 0.5%.

Solutions are kept in hermetically closed containers in a place protected from light; they are fit for use for several days.

SULFODIAMINE (Sulfodiaminum)

4,4'-bis Acetylamino phenyl sulfone



White, fine crystalline powder, odourless and tasteless, insoluble in water, almost insoluble in alcohol and the usual organic solvents. Melting point 286–291° (over a range of 2°).

Has been proposed for the treatment of whooping cough. When used during the first few days of the spasmodic period, a reduction in the number of attacks, a lowering of the temperature and an improvement in the general condition have been noted. When used early it has prevented the development of spasmodic coughing. When whooping cough is complicated with pneumonia, antibiotics must be prescribed simultaneously.

Administered orally in powder form (can be given with sugar syrup or porridge). Children up to 3 years old are given 0.1 g per kg body weight daily (the first administration should be a double one). Children from 3 to 6 years old are given single doses of 0.3–0.35 g from 6 to 12 years — 0.4 g. Course of treatment: 10–12 days. During the first 4 days the drug is given 5 times a day at 4 hour intervals; during the 5th–8th day — every 6 hrs, during the 9th–12th days — every 8 hrs.

Children not coughing who have been in contact with patients are given the drug 4 times a day (at intervals of 4 hrs) for 6 days children up to 3 years old are given a daily dose of 0.06 g per kg body weight, children from 3 to 6 years old are given single doses of 0.25 g, and children from 6 to 12 years old — 0.3 g

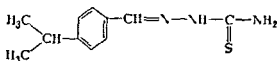
Cyanosis may develop during treatment this passes away when the drug is withdrawn If there should be cyanosis, administration is discontinued for 2—3 days when cyanosis disappears, the drug is again administered in half the dose. Treatment is to be carried out under the observation of a physician. Examinations of urine and blood are made during treatment (leukocyte count)

Contraindicated in decompensated heart disease severe anemia leukopenia and impairment of the function of liver and kidneys To be stored in a dark place, observing safety precautions (List B)

c) Thiosemicarbazones

CUTIZONE (Cutizonum)

Thiosemicarbazone of p isopropylbenzaldehyde



White crystalline powder sparingly soluble in water soluble in alcohol and acetone Melting point 147—151°

In experiments on white mice has chemotherapeutic activity in virus influenza When administered to influenza patients an abatement of symptoms of toxemia and a shortening of the period of fever have been noted

Administered orally in influenza, 3 times a day for 3—4 days Single doses for adults — 0.005 g Single doses for children from 1 to 3 years old — 0.001 g 3—5 years — 0.0015 g 5—7 years — 0.002 g, 7—10 years — 0.003 g 11—14 years — 0.004 g

Contraindicated in cases of impairment of liver function

Available in tablets

To be stored in a place protected from light observing safety precautions (List B)

II. ANTISEPTICS

A Antibiotics for external use

GRAMICIDIN S (Gramicidinum)

Soviet gramicidin (gramicidin S) is an antibiotic having a bacteriostatic and bactericidal action against streptococci staphylococci pneumococci the causative organisms of anaerobic infections and other microbes

Gramicidin is only used locally, intravenous injection is impermissible because of the possibility of hemolysis and phlebitis

Gramicidin S is available in the form of sterile 2% alcoholic solution in ampoules Ampoules should be opened under sterile conditions

The aqueous solution of gramicidin S used in practice is prepared by removing the contents of an ampoule with a syringe and diluting with 100 parts of sterile distilled or tap water Aqueous solutions are fit for use for 3 days The therapeutic alcoholic solution is prepared by diluting the contents of an ampoule with 100 parts of 70° alcohol The alcoholic solution may be kept for an unlimited period of time Oil solutions are prepared by diluting the initial alcoholic solution with 25—30 parts of castor oil, fish liver oil, lanolin or the like. Oil solutions

can be kept for a long time. The initial alcoholic solution in sealed ampoules can be kept for an unlimited time.

Aqueous solutions of gramicidin are used for moistening dressings, tampons, etc., in the treatment of suppurating wounds, bedsores, ulcers, osteomyelitis, wounds of the joints, empyema, complicated appendicitis, phlegmons, carbuncles, furuncles, etc. In treating wounds, oil solutions can be used after the disappearance of flora. In dermatological practice (in pyoderma), alcoholic solutions are used two applications per day.

Since gramicidin has a marked spermaticidal action, it is also used in the form of a paste as a contraceptive.

Gramicidin solution is to be stored in sealed ampoules in a place protected from light.

Rp Sol Gramicidini 2% 20
D t d N 6 in amp
S 2 ml to be diluted with 200 ml sterile
distilled water; for external use

Gramicidin contraceptive paste (Pasta Gramicidini) Composition 2% alcoholic gramicidin solution—9.89%, lactic acid—0.51%, emulsifier—15%; distilled water to make 100%.

Soft homogeneous white mass, thick consistency at room temperature but softens at body temperature and is easily distributed over the surface of the mucous membranes.

Available in tubes or jars with screw caps.

Introduced into the vagina with a special plastic syringe. Single dose—5–6 g.

POLYMYXIN M, sulphate (Polymyxinum).

Antibiotic substance produced by *Bacillus polymyxa*.

Structurally, polymyxin is a polypeptide.

Polymyxin sulfate: white powder, odourless, sweetish bitter taste, hygroscopic, freely soluble in water (1:3), sparingly soluble in alcohol, stable in weak acid and weak alkaline media.

The potency is determined biologically and is expressed in units of activity. 1 mg contains at least 8,000 units.

Polymyxin is only used topically; parenteral administration may lead to nephrotoxic and neurotoxic complications.

Polymyxin M acts chiefly on gram negative microbes, especially *Pseudomonas pyocyanea*. It also inhibits the growth of *coli* bacilli, typhoid and paratyphoid bacilli, and dysentery bacilli.

Used for irrigating, washing, swabbing, etc., in purulent processes, sluggishly healing wounds, abscesses, carbuncles, furuncles, pyodermatitis, purulent otitis, gangrenous putrefactive ulcers caused by an association of microbes with *Pseudomonas pyocyanea*.

Applied in the form of an aqueous solution containing 10,000–20,000 units per ml and ointments or emulsions containing 0.1, 0.5 and 1% polymyxin.

When applied topically there are no side effects. The drug should be used with caution in patients with disease of the kidneys, keeping constant watch on their function.

Available in hermetically sealed vials containing 500,000–1,000,000 units (0.05–0.1 g).

To be stored at a maximum temperature of 20°.

Aqueous solutions may be kept in the refrigerator at a temperature of +2–+8° for 7 days.

MICROCID (Microcidum)

Antibacterial preparation for external use. Acts on gram positive and gram negative microbes.

Transparent, almost colourless or slightly yellowish liquid Inactivated if heated above 41° Remains active at low temperatures

Used for the treatment of infected unhealing wounds, ulcers, bedsores, burns and eczema, as well as abscesses, phlegmons and other purulent inflammatory diseases

Used for moistening gauze dressings and tampons, for irrigating and washing Can also be applied in the form of a fish liver oil emulsion in cases of suppurating wounds, burns and frostbite Emulsions are prepared before use by shaking equal volumes of microcid and fish liver oil in a bottle

Used only topically Intravenous, subcutaneous and intramuscular injections, oral administration and instillation into cavities are impermissible

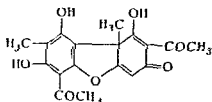
Available in bottles containing 100 and 200 ml.

To be stored in hermetically sealed bottles The contents of an open bottle must be used in 3 days Turbid preparations are unfit for use

SODIUM USNATE (*Natrium usnicum*)

Usnic acid pale lemon yellow crystalline substance Melting point 191—192° Isolated from lichens (*Ramalina reticulata* and others)

The following structure has been assigned to usnic acid



Usnic acid is an antibiotic substance which has an antimicrobial action against gram positive bacteria The sodium salt, which is used in medical practice, is a crystalline substance, soluble in water and alcohol Solutions are sterilized in the usual way

Used for the treatment of wounds, burns, fissures, etc.

Applied in the form of aqueous alcoholic or castor oil solutions, as well as in the form of glycerol or fir balsam solutions The drug is likewise used in powder form, alone or mixed with sulfanilamides (1 part sodium usnate with 3 or 5 parts sulfanilamide or norsulfazole)

Aqueous alcoholic solutions are prepared in the following way a 1—2% alcoholic solution is first prepared, and then mixed with 3—4 parts of 1% aqueous procaine hydrochloride solution

Castor oil solutions are prepared by adding small portions of a 10% alcoholic solution of the drug to castor oil that has been slightly warmed on the water bath, stirring the while A 50% alcoholic solution of ethyl aminobenzoate is added to the resulting oil solution

The castor oil solution is prepared with a content of 0.5—2% sodium usnate, ethyl aminobenzoate is added to give a concentration of 2% irrespective of the concentration of the antibiotic Purified tar can be added to the castor oil solution at the rate of 30 g per liter

Gauze dressings are thoroughly moistened with the solutions and applied to the affected areas of the skin

When dusting wounds with the powder, 0.1—0.2 g of the drug is used for a wound of about 16 cm² area

Before applying the drug, the wound or burnt surface must in all cases be given primary surgical treatment

IMANIN (*Imaninum*).

Antibacterial preparation for external use obtained from St Johnswort (*Hypericum perforatum* L.) (see p 206)

Dark brown powder, sparingly soluble in neutral water, freely soluble in alkaline water less soluble in alcohol, ether, acetone and glycerol

Acts mainly on gram positive bacteria. Along with its anti bacterial effect, imanin has the ability to dry wound surfaces and stimulate tissue regeneration.

Used as a local agent in the form of solutions, ointments and dusting powders for the treatment of fresh and infected wounds I and III degree burns ulcers abscesses phlegmons, pyoderma, carbuncles furuncles, mastitis, fissures of the nipples etc. Also used in acute pharyngitis, laryngitis, rhinitis and antritis.

A 1% aqueous solution is used for dressing wounds ulcers and other surface affections (if a 1% solution causes irritation, a 0.5% solution is used). Solutions are prepared in the following way 20 ml 0.1 N sodium hydroxide is added to 1 g imanin and heated on the water bath 5—10 min until the powder dissolves, after which the solution is made up to 100 ml with sterile distilled water.

Affected areas are washed or irrigated with the solution, and then covered with a damp dressing impregnated with the same solution. Dressings are changed daily or each second day, subsequently going over to ointment dressings (1 g imanin, 5 g lanolin, 15 g petrolatum).

For treating burns a 1% aqueous or aqueous alcoholic solution is used. The latter is prepared by boiling 1 g imanin with 20 ml 0.1 N sodium hydroxide 5—10 min after the powder dissolves, 30 ml water and 50 ml alcohol are added 5—10% ointments are also used.

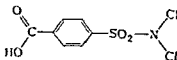
An aqueous glycerol solution can be used for swabbing the pharynx, it is prepared in the same way as the alcoholic solution.

Imanin is to be stored in hermetically closed bottles at a maximum temperature of 15°. On exposure to the air the potency of the preparation gradually diminishes. A 1% solution keeps its activity for 1—2 weeks.

B. Haloid group

HALAZONE (Halazonum)

p (Dichlorosulfamyl) benzoic acid



Synonyms Pantocid Pantosept

White powder with faint odour of chlorine, almost insoluble in water and dilute acids, freely soluble in solutions of caustic alkalis and carbonates. Contains at least 50% active chlorine.

Mostly used for disinfecting water, can be used for disinfecting the hands (1—1.5% solution) and for irrigating and washing wounds (0.1—0.5% solution). For disinfecting water, 1 tablet is used for 0.5—0.75 liter of water. The water is disinfected within 15 min. When water is strongly infected 2 tablets are used for the same amount. The taste of the water is not altered, there is only a slight odour of chlorine.

Available in tablets containing 0.0082 g halazone, 0.0036 g anhydrous sodium carbonate and 0.1082 g sodium chloride. Each tablet contains 3 mg active chlorine.

ALKALINE SODIUM HYPOCHLORITE

Synonym Antiformin

Yellowish liquid with odour of chlorine. Contains equal amounts of 20% sodium hypochlorite solution (NaOCl) and 15% sodium hydroxide solution.

Has a bactericidal action due to the chlorine content (about 5%) and to the evolution of nascent oxygen.

Used in dental practice as a disinfectant in the treatment of gingivitis and ulcerous stomatitis (10, 25 or 50% solution), and also in the laboratory for disinfecting discharges and infected material. Sometimes used as a skin lotion in pruritus.

Available in vials containing 50 ml

IODOFORM (Iodoformium) CHI_3

Synonyms Formyl triiodide, Formylum triiodatum, Triiodomethane

Lemon yellow, fine lustrous scales or fine crystalline powder, sharp characteristic, persistent odour, almost insoluble in water, sparingly soluble in alcohol (1:75), soluble in ether and chloroform, sparingly soluble in petrol and fatty and volatile oils.

Used externally as an antiseptic in the form of dusting powders, ointments, tampons, etc., in the treatment of infected wounds and ulcers.

Available in powder form

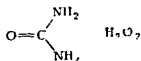
To be stored in well closed bottles in a cool place, protected from light

Also available in the form of a paste ready for use. Composition iodoform — 40 parts, zinc oxide — 40 parts, glycerol — 20 parts

C. Oxidizing agents

HYDROPERIT (Hydroperiti)

Tablets containing the complex compound of hydrogen peroxide and urea. Contains approx 35% hydrogen peroxide



Synonym Perhydrit

White tablets, freely soluble in water. The aqueous solution has a saline bitter taste. Each tablet weighs 1.5 g.

Used as an antiseptic in place of hydrogen peroxide

1 tablet corresponds to 15 ml (1 tablespoonful) 3% hydrogen peroxide solution. In order to obtain a solution corresponding to approximately 1% hydrogen peroxide solution, 2 tablets are dissolved in 100 ml of water. For gargling the mouth and throat, 1 tablet is dissolved in a glass of water (0.25% hydrogen peroxide solution).

Tablets are to be kept in well closed bottles in a dry place protected from light at a maximum temperature of 20°

POTASSIUM PERMANGANATE (Kalium hypermanganicum, Kalium permanganicum) KMnO_4

Dark or reddish violet crystals with metallic lustre, soluble in water (1:18 in cold and 1:3.5 in boiling water) forming dark purple solutions. Strong oxidizing agent. May explode on interaction with easily oxidized inorganic substances and organic materials (charcoal, sugar, tannin).

Used externally in the form of aqueous solutions as an antiseptic for washing wounds (0.1—0.5%), for gargling the mouth and throat (0.01—0.1%), for swabbing ulcers and burns (2—5%), for irrigating and washing in gynecological and urological practice (0.02—0.1%).

0.02—0.1% solutions are likewise used for stomach lavage in cases of poisoning from the oral ingestion of opium, morphine, aconitine and other alkaloids, strophanthine and phosphorus. Ineffective in poisoning with cocaine, atropine and barbiturates. Hydrocyanic acid is only oxidized by potassium permanganate in an alkaline medium.

D Acids and alkalis

SALICYLIC ACID (*Acidum salicylicum*)

o-Hydroxybenzoic acid



Fine white needles or light crystalline powder odourless sweetish taste Sparingly soluble in cold water (1:500), freely soluble in hot water (1:5) freely soluble in alcohol (1:3) and ether (1:2) Melting point 158—165°

Used externally as an antiseptic irritant counter irritant and keratolytic agent in the form of 2—5% dusting powders and 1—10% ointments pastes and alcoholic solutions

Corn Plaster of the following composition is available salicylic acid — 20 parts rosin — 27 parts paraffin wax — 26 parts petrolatum — 27 parts

BENZOIC ACID (*Acidum benzoicum*)



Colourless needles or fine white crystalline powder sparingly soluble in cold water (1:400), soluble in boiling water (1:25) soluble in alcohol (1:25) chloroform ether, benzene and fatty oils Melting point 122—124°

Used externally as an antiseptic When taken orally, stimulates secretion by the mucous membranes of the respiratory passages As an expectorant sodium benzoate is usually employed (see p 216)

BICARMINT

Tablets containing 0.4 g sodium borate 0.4 g sodium bicarbonate 0.2 g sodium chloride and 0.004 g menthol

Used as an antiseptic and antiphlogistic for gargling washing and inhaling in inflammatory processes of the upper respiratory passages 1—2 tablets are dissolved in 1/2 glass water

Available in glass tubes containing 10 tablets

E Salts of heavy metals

a) Mercury preparations

MERCURIC CHLORIDE Mercury bichloride (*Hydrargyrum bichloratum* *Hydrargyrum dichloratum* *Hydrargyrum sublimatum corrosivum*) $HgCl_2$
Synonyms Corrosive sublimate Mercury bichloride, Mercury chloride corrosive *Sublimatum Sulema*

Heavy white powder or white crystals soluble in cold water (1:185) more soluble in boiling water (1:3) soluble in alcohol (1:4) and ether (1:17) Aqueous solutions are acid Has a strong antiseptic action

Used in solutions (1:1000—1:500) for disinfecting underclothing and garments for washing walls and sick room articles and for disinfecting the skin Also used in the treatment of skin diseases and syphilis (in conjunction with novarsenol or myarsenol)

Available in tablets of 0.5 and 1 g consisting of equal parts of mercuric chloride and sodium chloride, tablets are coloured pink or reddish pink with 1% eosin solution

Mercuric chloride must be used with great caution because of the high toxicity, solutions may be absorbed and cause poisoning

Maximal doses for adults single—0.02 g daily—0.02 g

To be kept locked (List A)

MERCURIC OXYCYANIDE (*Hydrargyrum oxycyanatum*)

Basic mercuric cyanide, $\text{Hg}(\text{CN})_2 \cdot \text{HgO}$

White or slightly yellowish powder, sparingly soluble in water, insoluble in alcohol and ether. Aqueous solutions are alkaline

Used in a concentration of 1:5000—1:10,000 as a disinfectant lotion in blennorrhoea, gonorrhoea, conjunctivitis, dacrocystitis and cystitis

To be kept locked (List A) in well stoppered bottles of amber glass in a cool place, protected from light

MERCURIC CHLORIDE AMMONIATED Mercury white precipitate (*Hydrargyrum amidato chloratum*, *Hydrargyrum praecipitatum album*) HgNH_2Cl

Synonyms Aminomercury chloride Mercury cosmetic, White precipitate

White lumps or white amorphous powder, odourless, insoluble in water, alcohol and ether, soluble on warming in dilute hydrochloric nitric and acetic acids.

Used externally in the form of a 10% ointment (*White mercuric ointment*—*Ung Hydrargyri praecipitati albi*) as an antiseptic and antiphlogistic in skin diseases (pyoderma etc.)

To be stored in well stoppered bottles of amber glass in a place protected from light observing safety precautions (List B)

MERCURIC OXIDE YELLOW (*Hydrargyrum oxydatum flavum*, *Hydrargyrum praecipitatum flavum*) HgO

Heavy, extremely fine yellow powder, odourless insoluble in water, freely soluble in hydrochloric and nitric acids

Used in the form of a 2% ointment—*Yellow mercuric ointment*; *Eye ointment* (*Unguentum Hydrargyri oxydati flavi*, *Unguentum ophthalmicum*) Contains 1 part each of yellow mercuric oxide and liquid paraffin 40 parts petrolatum and 8 parts lanolin

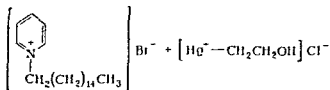
Applied in blepharitis, keratitis, conjunctivitis etc. and in skin diseases (sycosis seborrhoea)

When using yellow mercuric ointment in ocular practice it is not advisable to take bromides and iodides orally at the same time because of the possibility of mercuric bromide or iodide being formed in the eye—both compounds have a styptic action *Yellow mercuric ointment and ethylmorphine should not be used simultaneously because of the irritating effect*

To be stored in well stoppered bottles of amber glass in a place protected from light, observing safety precautions (List B)

DIOCID (*Drocidum*)

Mixture of cetylpyridinium bromide and ethanol mercury chloride



White powder, freely soluble in alcohol and hot water, less soluble in cold water. Solutions foam when shaken

D. Acids and alkalis

SALICYLIC ACID (*Acidum salicylicum*)

o Hydroxybenzoic acid



Fine white needles or light crystalline powder odourless sweetish sour taste Sparingly soluble in cold water (1:500), freely soluble in hot water (1:5) freely soluble in alcohol (1:3) and ether (1:2) Melting point 158—160.5°

Used externally as an antiseptic, irritant, counter irritant and keratolytic agent in the form of 2—5% dusting powders and 1—10% ointments pastes and alcoholic solutions

Corn Plaster of the following composition is available salicylic acid — 20 parts, rosin — 27 parts, paraffin wax — 26 parts, petrolatum — 27 parts.

BENZOIC ACID (*Acidum benzoicum*)



Colourless needles or fine white crystalline powder sparingly soluble in cold water (1:400), soluble in boiling water (1:25), soluble in alcohol (1:25), chloroform, ether, benzene and fatty oils Melting point 122—123°

Used externally as an antiseptic. When taken orally, stimulates secretion by the mucous membranes of the respiratory passages. As an expectorant, sodium benzoate is usually employed (see p. 216)

BICARMINT.

Tablets containing 0.4 g sodium borate, 0.4 g sodium bicarbonate, 0.2 g sodium chloride and 0.004 g menthol

Used as an antiseptic and antiphlogistic for gargling, washing and inhaling in inflammatory processes of the upper respiratory passages. 1—2 tablets are dissolved in 1/2 glass water

Available in glass tubes containing 10 tablets

E. Salts of heavy metals

a) Mercury preparations

MERCURIC CHLORIDE, Mercury bichloride (*Hydrargyrum bichloratum*, *Hydrargyrum dichloratum*, *Hydrargyrum sublimatum corrosivum*) HgCl_2

Synonyms Corrosive sublimate, Mercury bichloride, Mercury chloride corrosive Sublimate Sulema

Heavy white powder or white crystals soluble in cold water (1:185) more soluble in boiling water (1:3), soluble in alcohol (1:1) and ether (1:17) Aqueous solutions are acid Has a strong antiseptic action

Used in solutions (1:1000—1:500) for disinfecting underclothing and garments for washing walls and sick room articles and for disinfecting the skin. Also used in the treatment of skin diseases and syphilis (in conjunction with not arsenol or myarsenol)

Available in tablets of 0.5 and 1 g consisting of equal parts of mercuric chloride and sodium chloride tablets are coloured pink or reddish pink with 1% eosin solution

Mercuric chloride must be used with great caution because of the high toxicity, solutions may be absorbed and cause poisoning

Maximal doses for adults single—0.02 g daily—0.02 g

To be kept locked (List A)

MERCURIC OXYCYANIDE (Hydrargyrum oxycyanatum)

Basic mercuric cyanide $\text{Hg}(\text{CN})_2 \cdot \text{HgO}$

White or slightly yellowish powder sparingly soluble in water insoluble in alcohol and ether Aqueous solutions are alkaline

Used in a concentration of 1:5000—1:10000 as a disinfectant lotion in blennorrhoea gonorrhoea conjunctivitis dacryocystitis and cystitis

To be kept locked (List A) in well stoppered bottles of amber glass in a cool place protected from light

MERCURIC CHLORIDE AMMONIATED Mercury white precipitate (Hydrargyrum amidato chloratum Hydrargyrum praecipitatum album) HgNH_2Cl

Synonyms Aminomercury chloride Mercury cosmetic White precipitate

White lumps or white amorphous powder odourless insoluble in water alcohol and ether soluble on warming in dilute hydrochloric nitric and acetic acids.

Used externally in the form of a 10% ointment (White mercuric ointment—Ung Hydrargyri praecipitati albi) as an antiseptic and antiphlogistic in skin diseases (pyoderma etc)

To be stored in well stoppered bottles of amber glass in a place protected from light observing safety precautions (List B)

MERCURIC OXIDE YELLOW (Hydrargyrum oxydatum flavum Hydrargyrum praecipitatum flavum) HgO

Heavy extremely fine yellow powder odourless insoluble in water freely soluble in hydrochloric and nitric acids

Used in the form of a 2% ointment—Yellow mercuric ointment, Eye ointment (Unguentum Hydrargyri oxydati flavi Unguentum ophthalmicum) Contains 1 part each of yellow mercuric oxide and liquid paraffin 40 parts petrolatum and 8 parts lanolin

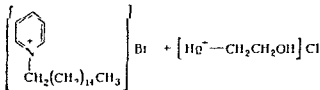
Applied in blepharitis keratitis conjunctivitis etc and in skin diseases (sycosis seborrhoea)

When using yellow mercuric ointment in ocular practice it is not advisable to take bromides and iodides orally at the same time because of the possibility of mercuric bromide or iodide being formed in the eye—both compounds have a styptic action Yellow mercuric ointment and ethylmorphine should not be used simultaneously because of the irritating effect

To be stored in well stoppered bottles of amber glass in a place protected from light observing safety precautions (List B)

DIOCID (Diocidum)

Mixture of cetylpyridinium bromide and ethanol mercury chloride



White powder freely soluble in alcohol and hot water less soluble in cold water Solutions foam when shaken

Also available in separate tablets. No 1 tablets contain 0.32 g cetylpyridinium bromide and No 2 tablets of smaller diameter contain 0.35 g ethanol mercury chloride.

Ethanol mercury chloride is a powerful mercury antiseptic. Cetylpyridinium bromide is a quaternary ammonium compound belonging to the class of cation (invert) soaps. These substances (detergents) possess great surface activity and have a washing and disinfectant action. It must be borne in mind that cation soaps are less active in the presence of anion detergents such as ordinary soaps. They are also less active in the presence of serum and other organic substances.

Diocid which combines the properties of cetylpyridinium bromide and ethanol mercury chloride is a good washing and antibacterial agent.

In surgery diocid solutions are used for washing the hands before operations. A 1:5000 solution of diocid in boiled warm water is poured into a sterilized enamelled basin, the hands are washed for 3 min with a sterile gauze napkin, wiped with a sterile napkin and rubbed for 2 min with a sterile napkin moistened with 96° ethyl alcohol. The hands and fingers should not be painted with iodine because of the danger of irritating the skin.

When separate tablets are available a 1:5000 solution is prepared by dissolving 2 cetylpyridinium bromide tablets and 1 ethanol mercury chloride tablet in 5 liters of water. It is advisable to first pulverize the tablets. Solution in warm water requires 10—15 min.

In a concentration of 1:5000 diocid keeps the skin aseptic for at least 2 hrs without causing irritation. Stronger concentrations may cause irritation and dry the skin. A concentration of 1:2500 is used if the hands have been contaminated with purulent discharges.

Diocid is also a highly effective agent for disinfecting pharmaceutical ware. Such ware is made sterile by holding 1 hr in a 1:5000 solution of diocid (G. A. Vaisman and O. N. Sosnova).

A 1:5000 solution is also recommended for pharmacists' assistants for washing the hands before preparing medicines.

To be kept locked (List A) in a dry place.

b) Silver preparations

SILVER PROTEIN (*Argentum proteinicum*)

Synonym Prolargol

Brownish yellow or yellow light powder, odourless, slightly bitter and slightly astringent taste, freely soluble in water, insoluble in alcohol, ether and chloroform. Contains 78—83% silver.

Used as an astringent, antiseptic and antiphlogistic for painting the mucous membranes of the upper respiratory passages (1—5% solution) for irrigating the urethra and bladder in chronic gonorrheal urethritis (1—3% solution) as eyedrops in conjunctivitis, blepharitis and blennorrhea (1—3% solution).

Available in powder form.

To be stored in well closed bottles of amber glass in a place protected from light.

COLLOIDAL SILVER (*Argentum colloidal*)

Synonym Collargol

Greenish black or bluish black platelets with metallic lustre, soluble in water with the formation of a colloidal solution. Contains 70% silver.

Use: 1) in the form of a 0.2—1% solution for irrigating suppurating wounds; 2) 1—2% solution for irrigating the bladder in chronic cystitis and urethritis; 3) 2, 3 or 5% solution for eyedrops in purulent conjunctivitis and blennorrhea; 4) at times in the form of a 2% solution as a warm enema (50 ml) in bacillary dysentery. A 15% ointment is sometimes applied in erysipelas, lymphangitis and soft chancre. 3 g is used for adults, 1—4 times a day; 1 g—for children. In sepsis intravenous injections of 2—10 ml 2% solution.

are sometimes given for 5—8 days Freshly prepared solutions are used for injections to be injected slowly

Maximal doses intravenously for adults single—0.25 g daily—0.5 g

Available in powder form

To be stored in well stoppered bottles or sealed ampoules of amber glass in a place protected from light observing safety precautions (List B)

BACTERICIDAL PAPER

Porous paper impregnated with silver nitrate and silver chloride

Used for disinfecting small wounds abrasions and II degree burns when opening blisters

The bactericidal paper is slightly moistened with distilled or tap water applied to the affected area covered with a thin layer of cotton and fixed in place with a bandage If wounds are bleeding it is not necessary to moisten the paper

Available in envelopes containing sheets of paper 10×14 cm in size

In out patient clinics to be kept in jars of porcelain or dark brown glass in field or home conditions to be kept in the original package

c) Lead preparations

LEAD PLASTER SIMPLE (Emplastrum plumbi simplex Emplastrum diachylon simplex)

Composition lead oxide—10 parts lard—10 parts sunflower seed oil—10 parts sufficient water to form a homogeneous plastic mass

Used in purulent inflammatory skin diseases furuncles carbuncles etc

d) Zinc preparations

ZINC SULFATE (Zincum sulfuricum Zinci sulfas)



Colourless transparent prisms or fine crystalline powder odourless astringent metallic taste very freely soluble in water insoluble in alcohol Aqueous solutions are acid

Used as an antiseptic and astringent in conjunctivitis (0.1–0.25 and 0.5% eyedrops) chronic catarrh of laryngitis (0.25–0.5% solution for swabbing or pulverization) urethritis and vaginitis (0.1–0.5% solution for irrigation) In rare cases administered orally as an emetic in a dose of 0.1–0.3 g

Maximal single dose for adults as emetic (orally) 1 g

Available in powder form

To be stored in well stoppered bottles observing safety precautions (List B)

Rp Sol Zinci sulfurici 0.25% 100

DS Eyedrops (2 drops in eye twice a day)

Rp Zinci sulfurici

Plumbi acetici 33 0.3

Aq destill 200.0

MDS For irrigating

Rp Zinci sulfurici 0.025

Sol Acidi boric 2% 100

MDS Eyedrops (2 drops in eye twice a day)

F Formaldehyde group

LYSOFORM (Lysoformium)

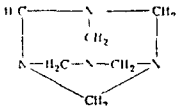
Soap solution of formaldehyde Composition Formaldehyde solution—40 parts potassium soap—40 parts alcohol—20 parts

Transparent yellowish brown solution with odour of formaldehyde miscible with water in all proportions Disinfectant and deodorant

Used for irrigating in gynecological practice (1–1% aqueous solutions) and for disinfecting hands and premises (1–3% solution)

METHENAMINE (Methenaminum)

Hexamethylenetetramine



Synonyms Aminoform Cystamine Cystogen Formamin Formin Hexamethylentetramin Hexamina Metramine Urisol Uritone Urotropine Vesalvine

Colourless crystals or white crystalline powder odourless pungent sweet and then bitterish taste freely soluble in water (1:15) and alcohol (1:10) On heating sublimates without melting Burns with a pale flame

Aqueous solutions are alkaline Solutions for intravenous injections are prepared aseptically and are not sterilized

Used as a disinfectant the drug being hydrolyzed in an acid medium with the liberation of formaldehyde

Administered orally in the form of powders tablets and solutions The dose for adults is 0.5–1 g that for children 0.1–0.5 g Taken several times a day Intravenously injections of 5–10 ml 40% solution are given

Indications cystitis pyelitis and other inflammatory diseases of the urinary tract cholecystitis and cholangitis allergic skin diseases (urticaria erythema multiforme etc) ocular diseases (iridocyclitis keratitis etc) Also used in meningitis encephalitis arachnoiditis and rheumatism

When using methenamine for the treatment of diseases of the urinary tract it should be borne in mind that formaldehyde is not split off in an alkaline medium of the urine and the drug has no therapeutic effect In such cases substances are prescribed to shift the reaction of the urine toward the acid (ammonium chloride monobasic sodium phosphate)

Methenamine may irritate the parenchyma of the kidneys and in some cases lead to the extension of the pathological process in pyelitis If symptoms of irritation of the kidneys are detected administration of the drug is discontinued

Available in powder form, in tablets of 0.25 and 0.5 g and in ampoules containing 5 and 10 ml 40% solution Compound tablets are also available containing 1) 0.25 and 0.5 g methenamine and 0.25 and 0.5 g salol 2) 0.25 g methenamine and 0.015 g Belladonna extract

CALCEX TABLETS (Tabulettae "Calcex")

White tablets with crystalline fracture saline bitter taste freely soluble in water

Contain 0.5 g of the complex salt of methenamine and calcium chloride.

1–2 tablets are taken 3–4 times a day in cases of cold

G Phenol group

RESORCINOL (Resorcīnolum) m Dihydroxybenzene



Synonym Resorcin

Yellowish or greyish white crystalline powder gradually becoming pink under the influence of light and air faint characteristic odour very freely soluble in water (1 1) and alcohol (1 1) freely soluble in ether and glycerol soluble in fatty oils (1 20) very slightly soluble in chloroform Incompatible with alkalis

Used topically in skin diseases (eczema seborrhea pruritus fungous diseases) in the form of 2—5% aqueous and alcoholic solutions and 5—10% ointments Less frequently administered orally as a disinfectant in gastrointestinal diseases

Single dose for adults 0.25—0.3 g Doses for children 0.01—0.1 g depending on the age

ICHTHAMMOL (Ichthammolum)

Ammonium salt of the sulfonic acids of shale oil (Ammonium sulfoichthylolum)

Synonyms Bitaminolum Bithiolum Ichtham Ichthyol Ichthyolammum Ichtyopan Ichtyosulfol Isarol

Almost black syrupy liquid (in thin layer brown) characteristic sharp odour and taste soluble in water and glycerol partially soluble in alcohol and ether Aqueous solutions foam to a marked degree when shaken

Ichthammol contains 10.5% organic sulfur Solutions are incompatible with iodides alkaloids and the salts of heavy metals

Has an antiphlogistic analgesic and to some extent an antiseptic action

Used topically in skin diseases (burns erysipelas eczema etc) and in neuralgia arthritis etc in the form of 5—30% ointments or 10—30% aqueous alcoholic lotions In inflammatory diseases of the pelvic organs (metritis parametritis salpingitis prostatitis etc) suppositories or tampons moistened with a 10% glycerol solution of ichthammol are prescribed

Available in glass jars The following preparations are available ready for use Ichthammol Naftalan Petroleum Paste (ichthammol—4 parts zinc oxide—10 parts naftalan petroleum ointment—16 parts starch—10 parts) Ichthammol Ointment (10% and 20%) on a petrolatum base Ichthammol Suppositories (ichthammol—0.2 g fatty base—1.2 g) in boxes of 10

ALBICHTHOL (Albichtholum)

Rectified light oil from shale tar mixture of thiophene homologues with admixture of hydrocarbons Contains at least 9% sulfur Transparent, yellowish or greenish mobile volatile liquid with characteristic disagreeable odour Gradually turns red on exposure to air Burns with sooty flame Insoluble in water soluble in chloroform turpentine and benzene Specific gravity—0.89—0.925 Action similar to that of ichthammol but less irritating to skin and does not soil underclothes

Used in skin diseases in the form of 2 5 10 and 15% ointments on a petrolatum base and in inflammatory diseases of the pelvic organs in the form of suppositories and globules

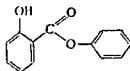
For the control of lice **Albichthol Paste** is used (a mixture of albichthol and green soap) the paste destroys lice bedbugs and cockroaches

Applied to the hairy parts of the body in the form of a 50% aqueous emulsion (prepared with warm water) The hairy parts are thoroughly wet with the emulsion and in 10—15 min washed with warm water and combed

A 10% aqueous emulsion is used for disinfecting underclothes and premises underclothes are immersed in the emulsion for 15 min

SALOL (Salolum)

Phenylsalicylate



Synonym Musol

White crystalline powder or fine colourless crystals faint odour almost insoluble in water soluble in alcohol (1:10) freely soluble in ether and chloroform Melting point 42—43°

Administered orally in powders or tablets (often in combination with other drugs) in intestinal diseases as well as in cystitis and pyelitis and pyelonephritis In the alkaline contents of the intestine salol is hydrolyzed into salicylic acid and phenol which have a certain antiseptic action on the intestinal flora Salicylic acid and phenol are partially excreted by the kidneys and may have some disinfecting influence on the flora of the urinary tract

Salol has only a weak antimicrobial action

Administered in doses of 0.3—0.5 g 3—4 times a day often in combination with other drugs

Availability — powder and various compound tablets

a) salol — 0.25 g (0.5 g) bismuth — 0.25 g (0.5 g)

b) salol — 0.25 g (0.3 or 0.5 g) methenamine — 0.25 g (0.3 or 0.5 g)

c) salol — 0.25 g bismuth — 0.25 g Belladonna extract — 0.015 g

d) salol — 0.3 g Belladonna extract — 0.01 g (Besalol — Besalolum)

e) salol — 0.25 g methenamine — 0.25 g Belladonna extract — 0.015 g (Urobesalol — Urobesalolum)

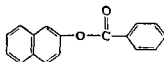
f) salol — 0.5 g methenamine — 0.5 g Belladonna extract — 0.02 g

g) salol — 0.3 g albumin tannate — 0.3 g (Tansal — Tansalum)

h) salol — 0.2 g benzonaphthol — 0.2 g Belladonna extract — 0.15 g

BENZONAPHTHOL (Benzonaphtholum)

β — Naphthyl benzoate



Fine white crystalline powder odourless and tasteless insoluble in water soluble in boiling alcohol (1:8) and in ether (1:30) Melting point 107—109°

Used orally as an antiseptic in diseases of the gastrointestinal tract Adults are given doses of 0.3—0.5 g 3—4 times a day Doses for children up to 1 year old — 0.05 g 1—2 years — 0.1 g 3—4 years — 0.15 g 5—6 years — 0.2 g 7 years — 0.25 g 8—14 years — 0.3 g

Available in powder form and in tablets of 0.25 and 0.5 g

To be stored in well stoppered bottles in a place protected from light.

H Petroleum products Mineral oils Balsams

NAFTALAN PETROLEUM REFINED (Naphthalanum liquidum raffinatum)

Complex mixture of hydrocarbons and tars Thick black syrupy liquid with greenish fluorescence characteristic odour, weakly acid reaction

Specific gravity—0.925—0.960 **Immiscible** with water, freely soluble in petrol, chloroform and benzene, miscible with glycerol, oils and fats

Naftalan (Naphthalanum) or **Naftalan Ointment** (Unguentum naphthalani) is a mixture of 70 parts refined naftalan petroleum, 18 parts paraffin wax and 12 parts petrolatum. Homogeneous black mass with odour of naftalan petroleum. Insoluble in water but on grinding, mixes with water up to 35%, sparingly soluble in alcohol. Miscible on grinding, with glycerol, fats and oils.

Naftalan emulsion (Emulsum naphthalani liquidi) 10% aqueous emulsion of refined naftalan petroleum. Syrupy black liquid with greenish fluorescence and characteristic odour, weakly acid reaction, immiscible with water.

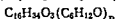
Naftalan petroleum and preparations obtained from it have an emollient, resolving, disinfecting and slightly analgesic action on the skin and mucous membranes.

Like other agents used on the skin they may have a general reflex influence on the organism.

Use skin diseases (eczema neurodermatitis, furunculosis, erysipelas etc.), inflammatory diseases of the joints and muscles (arthritis osteoarthritis myalgia, etc.), neuralgia, radiculitis and plexitis, burns ulcers, bedsores, etc.

Applied alone or in combination with other drugs in the form of ointments, pastes and suppositories. Naftalan emulsion is also used for irrigating, compresses, tampons, baths and galvanization.

VINYLIN; Shostakovsky's Balsam (Vinylinum Balsamum Schostakowsky) Polyvinylbutyl ether (Aether polyvinylbutylicus)



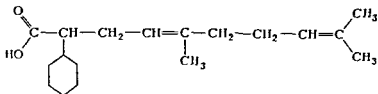
Light yellow, thick, viscous liquid, specific odour, insoluble in water, miscible with chloroform, ether and vegetable and mineral oils.

Used for treating furuncles, carbuncles, trophic ulcers, suppurating wounds, mastitis, wounds of the soft tissues, burns, frostbite and inflammatory diseases. Promotes the cleaning of wounds, tissue regeneration and epithelization.

Used externally for moistening dressings and for applying directly to the wound surface, per se and in the form of 20% oil solutions as well as ointments. Administered orally in ulcer of the stomach and duodenum, gastritis and colitis. Dose from 1 teaspoonful to one dessertspoonful once a day, to be taken 5—6 hrs after meals.

CYGEROL (Cygerolum)

(±) di 2 Cyclohexyl 5.9 dimethyl Δ^{4.8} capric acid



Light yellow, transparent, oily liquid of the consistency of glycerol, faint characteristic odour, bitterish taste, insoluble in water, soluble in organic solvents. Sterilized by the usual methods.

Applied topically in the treatment of granulating wounds, trophic ulcers, burnt surfaces, etc.

A sterile gauze dressing is moistened with cygerol, applied to the wound surface and covered with compress paper. If the wound surface is large and there is a copious discharge, compress paper is not used. The wound or ulcer is cleaned from pus before applying cygerol. When treating large wound surfaces (over 20 cm² in area), cygerol is diluted 1:5 with sterile vegetable oil. Dressings are usually changed in 1—2 days, in burns in 4—5 days.

Cygerol does not take the place of surgical treatment

When cygerol is applied to large wound surfaces it causes a burning sensation

POLYMEROL (Polymerolum)

Polymerized "Avtol" cylinder oil Dark brown syrupy liquid with odour of over heated oil Insoluble in water and alcohol soluble in ether chloroform and benzene

Used externally as an ointment and for moistening dressings in streptoder matitis chronic eczema pyoderma fissures of the nipples burns etc Applied once a day

Contraindicated in dermatoses caused by oils To be stored in well stoppered bottles

AVTOL OINTMENT (Unguentum autoli)

Composition engine oil or "Avtol" cylinder oil—85 parts stearin—12 parts zinc oxide—3 parts Alternative composition cylinder oil—85 parts stearin—7 parts paraffin wax—3 parts lard—5 parts

Brownish yellow or chocolate coloured ointment odourless

Used for the treatment of wounds ulcers and burns and as a base for other ointments (see Antipsoriaticum)

BF 6 CEMENT

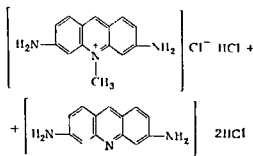
Alcoholic solution of a special synthetic resin Quickly dries when applied to the skin forming a thin elastic film

Used for covering small wounds abrasions and fissures The cement is applied to the wound and surrounding skin with a glass rod the cement dries in 3—5 min forming a film No bandage is applied The film usually remains intact for 2—3 days after which it begins to come off If the wound has not healed by that time the old film is removed and a fresh one applied The cement must not be applied to contaminated wounds to inflamed skin or to wounds that are bleeding

1 Dyes

ACRIFLAVINE (Acriflavinum) Flavacridine hydrochloride

A mixture of the hydrochloride of 3,6-diamino-10-methyl-acridinium chloride and the dihydrochloride of 3,6-diaminoacridine



Synonyms Acriflavini chloridum Chromoflavine Euflavin Flavine Flavipin Gonocrin Neutraflavin Panflavin Trypaflavine Xanthaeridinum

Orange red or brownish red crystalline powder odourless freely soluble in water (1:3) sparingly soluble in 95° alcohol sparingly soluble in ether and

chloroform Aqueous solutions are acid, they are sensitive to light and must be kept in a dark place in sealed dark ampoules or bottles of dark amber glass

Acriflavine has bactericidal properties it acts on diphtheria bacilli and cocci (streptococci, staphylococci, meningococci and gonococci), it does not inhibit phagocytosis nor irritate the tissues The bactericidal action is not weakened in the presence of blood serum The drug destroys the causative organisms of piroplasmosis in animals

Acriflavine solutions are used locally, and at times are injected intravenously, they are not injected subcutaneously since they irritate the tissues

Used locally in the form of a 0.1% solution in isotonic saline for irrigating and washing infected wounds and ulcers, abscesses phlegmons, etc A 0.1% aqueous solution is used for gargling and rinsing in cases of catarrhal inflammation of the mucous membrane of the mouth nose, and pharynx Sometimes administered intravenously in sepsis, endocarditis, erysipelas and meningitis Treatment is begun with the injection of 5—10 ml 0.5% solution, going over to the administration of 1 or 2% solution after 2—3 injections Injections are given once in 2—3 days The course consists of 5—10 injections Solutions are first warmed to 37°, and are injected slowly

The same course of intravenous injections of acriflavine is recommended in nonspecific inflammatory diseases of the urinary tract (cystitis pyelitis) Intravenous administration can be combined with irrigation of the pelvis and bladder with a 0.2% solution Usually there is no irritation of the kidneys

When the drug is rapidly injected intravenously it may give rise to headache and general lassitude Excreted by the kidneys, the urine becoming greenish in colour Excretion after a single injection continues 36—48 hrs

Available in powder form

To be stored in well stoppered bottles of amber glass observing safety precautions (List B)

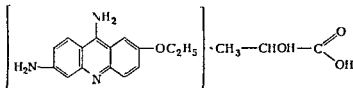
TRIPAZOL TABLETS

Contain acriflavine, boroverin (methenamine triborate), menthol, eucalyptus oil, sugar and cocoa average weight 0.55 g

To be sucked, as an antiseptic in inflammatory diseases of the mouth and throat

ETHACRIDINE (Aethacridinum)

2 Ethoxy 6 9 diaminoacridine lactate



Synonyms Acracidum, Acrinol, Acrinolin, Ethodin Rivanol

Fine yellow crystalline powder, odourless, bitter taste sparingly soluble in cold water (1:50), more soluble in hot water, sparingly soluble in alcohol (1:110), practically insoluble in ether Aqueous solutions are unstable, especially on exposure to light (become brown)

Only freshly prepared solutions should be used

Has an antimicrobial action for the most part in infections caused by cocci, especially streptococci The drug is only slightly toxic and does not irritate the tissues

Used as a preventive and therapeutic antiseptic in surgery, gynecology, urology, ophthalmology, dermatology and otolaryngology. For treating fresh and infected wounds aqueous solutions are used 0.05% (1:2,000), 0.1% and 0.2%. For irrigating the pleural and abdominal cavities in purulent pleuritis and peritonitis, as well as in purulent arthritis and cystitis 0.05—0.1% solutions are used. In cases of furuncles, carbuncles and abscesses 0.1—0.2% solutions are applied in the form of lotions and tampons. A 0.1% solution is used for irrigating the uterus in the puerperal period, in coccal conjunctivitis a 0.1% solution is applied in the form of eyedrops. In inflammation of the mucous membrane of the mouth, pharynx and nose, rinsing or gargling with a 0.1% solution is prescribed, or the mucosa is swabbed with a 1% solution. In dermatology, 2.5% dusting powders, 1% ointment and 5—10% pastes are used.

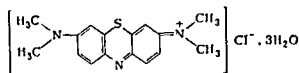
Maximal doses for adults: single—0.05 g, daily—0.15 g.

Irrigation of cavities is contraindicated in cases of impaired kidney function when albumin is present in the urine.

Available in powder form and in tablets of 0.1 g.

To be stored in well stoppered bottles, observing safety precautions (List B).

METHYLENE BLUE; Methylthionine chloride (Methylenum coeruleum, Methylenblau, Methylthionil chloridum).
Tetramethylthionine chloride



Dark green crystalline powder or dark green crystals with bronze lustre, soluble in water (1:30), sparingly soluble in alcohol, insoluble in ether. Aqueous solutions are blue. Sterilized with running steam at a temperature of 100° for 30 min.

Used topically in the form of 1—3% alcoholic solutions as an antiseptic in burns, pyoderma, folliculitis, etc. In cystitis, urethritis and the like a 0.02% (1:5,000) aqueous solution is used for irrigation.

Administered orally in cystitis, urethritis and other inflammatory diseases of the urinary tract. Adults are given 0.1 g 3—4 times a day, children, 0.005—0.01 g for each year of their age, the daily dose being divided for 3—4 administrations. The drug is likewise used for testing the functional ability of the kidneys but more precise results are obtained if Indigo Carmine is used for this purpose (see p. 436).

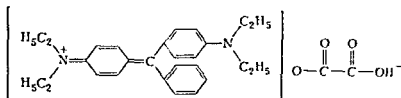
Methylene blue has oxidizing-reducing properties and can act as the acceptor or donor of hydrogen in the organism, this is the basis for its use as an antidote in some cases of poisoning. Solutions of methylene blue are administered intravenously in poisoning with cyanides, carbon monoxide and hydrogen sulfide. Dose: 50—100 ml 1% aqueous solution or 1% methylene blue solution in 25% glucose ("chromosmon"). The therapeutic action in poisoning with hydrocyanic acid is based on the ability of methylene blue to convert hemoglobin into methemoglobin which combines with cyanides.

When methylene blue is injected intravenously in small doses (0.1—0.15 ml 1% solution per kg body weight), methemoglobin is reduced to hemoglobin. This property of methylene blue is taken advantage of in poisoning with methemoglobin-forming poisons (nitrites, aniline and its derivatives, etc.).

Available in powder form and in ampoules containing 20 and 50 ml 1% methylene blue solution in 25% glucose.

BRILLIANT GREEN (Viride nifens, Brillantgrün)

Tetraethyldiaminotriphenylmethane oxalate



Greenish golden lumps or golden green powder, soluble in water (1:50), sparingly soluble in alcohol, solutions are of an intense green colour

Used externally as an antiseptic in the form of a 0.1–2% alcoholic or aqueous solution for painting affected areas in pyoderma, blepharitis, etc.

Available in powder form

NOVIKOV'S ANTISEPTIC LIQUID

Composition: tannin—1 part, brilliant green—0.2 part, 96° alcohol—0.2 part, castor oil—0.5 part, collodion—20 parts

Colloidal mass which dries quickly, forming a dense, elastic film on the skin

Proposed as an antiseptic agent for treating minor skin injuries. The skin surrounding the affected spot is cleaned, wiping it off with petrol when necessary (when contaminated with oils). Novikov's liquid is then applied directly to the injured area and the surrounding skin.

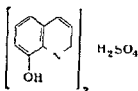
The liquid must not be used on wounds that are bleeding profusely or that are infected.

The liquid is flammable. It must be kept in containers with ground glass or rubber stoppers, and away from fire.

J. Hydroxyquinoline derivatives

HYDROXYQUINOLINE

8-Hydroxyquinoline sulfate



Synonyms: Chinosol, Cryptonol, Idril, Oxyquinol, Quinozol, Soloxin, Soliquinate, Sunoxol, Superol.

Lemon yellow, fine crystalline powder, characteristic odour, freely soluble in water (1:13), sparingly soluble in alcohol, insoluble in ether. Melting point 175–178°.

Has relatively low toxicity, does not irritate the tissues and is not inactivated by the tissue proteins.

Used in a dilution of 1:1,000–1:2,000 for disinfecting the hands, for washing wounds and ulcers and for irrigating; it is also used in the form of 1–2% dusting powders and 5–10% ointments.

It cannot be used for disinfecting medical instruments since it reacts with metals.

Hydroxyquinoline is one of the ingredients of the contraceptive preparation "Contraceptin".

To be stored in well stoppered glass bottles

CONTRACEPTIN

Contraceptive preparation Globules of the following composition hydroxy

quinoline—0.03 g boric acid—0.1 g tannin—0.06 g fatty base—1.7 g

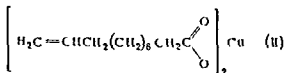
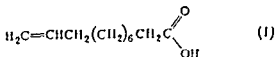
Introduced into the vagina 5—6 min before coitus

K Preparations used in the treatment of fungous skin diseases

UNDECIN (Undecinum)

Ointment consisting of 8% undecylenic acid (I) 8% copper undecylenate

(II) 4% glyceryl p chlorophenyl ether and 80% base



Has fungistatic and fungicidal properties

Used in the treatment of fungous affections of the skin (epidermophytosis pityriasis versicolor etc) Less effective in fungous affections of the hair

Applied to the affected areas of the skin twice a day for 1½—2 weeks or more, depending on the time necessary for the disappearance of the pathogenic fungi

ZINCUNDAN (Zincundanium)

Ointment containing 5% undecylenic acid 10% zinc undecylenate 10% salicylanilide and 75% base (non fatty)

Used for the treatment of fungous skin diseases (epidermophytosis yeast dermatoses etc)

The ointment is rubbed into the affected areas of the skin 15—20 days or more depending on the form and course of the disease. During treatment and afterwards it is advisable to dust the affected areas with "Dustundan"

DUSTUNDAN (Dustundanium)

Powder containing 5% undecylenic acid 10% zinc undecylenate, 10% salicylanilide and 75% talc.

Used for the prevention and treatment of fungous skin diseases (see Zincundan) The affected areas of the skin are powdered with the preparation it is also sprinkled inside socks stockings and shoes

THALLIUM PLASTER (Emplastrum thalii)

A preparation facilitating the therapy of fungous skin diseases its use is based on the ability of thallium to cause the hair to fall out (epilation)

Chiefly used for epilation in fungous diseases of the hairy part of the head as well as the areas of the beard moustaches and brows

3 and 5% thallium plaster is used

Composition thallium acetate—3 parts for 3% or 5 parts for 5% plaster simple lead plaster—62 parts for 3% or 60 parts for 5% yellow wax—5 parts anhydrous lanolin—20 parts water—10 parts Light yellow or brownish yellow homogeneous sticky mass of soft consistency 1 g 3% plaster contains 0.03 g thallium acetate 1 g 5% plaster—0.05 g thallium acetate

When using the plaster the dose of thallium acetate should not exceed 0.013 g per kg body weight. Higher doses are impermissible because of the danger of toxic manifestations.

When there are a large number of affected areas (on the hairy part of the head) it is best to use the 3% plaster. In solitary foci of infection only enough plaster is used to cover the entire affected area with a thin layer. When there are a large number of foci over the entire hairy part of the head the plaster may be applied successively in several administrations so as finally to treat all the affected areas. Each time the amount of plaster permissible for the patient's weight is used. Between successive administrations there should be an interval of at least 5—7 days.

Before applying the plaster the head is shaved and washed with soap and warm water. The plaster is slightly warmed and applied to the affected foci and for 1 cm around them with a metal or glass spatula. After applying the plaster overlapping strips of sticking plaster are placed over the affected areas. The application of a gauze bandage is also recommended. The plaster is left 20 days. During that time 10% sulfur tar ointment is applied daily to the healthy areas of the hairy part of the head. In 20 days the plaster is removed after which a pressure dressing of 2—5% salicylic petrolatum is applied to the affected areas and left for 24 hrs. This is followed by careful manual depilation and iodine ointment treatment for 1½ months the skin is painted with 2% tincture of iodine in the morning and in the evening 15% sulfur tar ointment is rubbed in. Besides this the "exfoliation" method proposed by A. M. Arievich is used: a pressure dressing with an ointment containing 12% salicylic and 6% lactic (or benzoic) acid in petrolatum is applied to the foci of infection and left for 2 days. When this dressing is removed another dressing with 2% salicylic petrolatum is immediately applied and left for 24 hrs. Ointment with salicylic and lactic acid is applied once in 7—10 days.

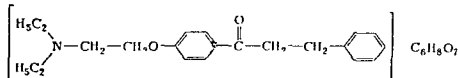
After the first exfoliation tests for the fungi are carried out every 7—10 days. Iodine ointment treatment is discontinued after 2 negative tests for the fungi have been obtained.

The use of thallium plaster is contraindicated in diseases of the liver and kidneys and in rheumatism and gastrointestinal disorders. Before treatment blood and urine examinations must be made and the patient must be weighed.

To be stored in well stoppered glass bottles in a cool place protected from light observing safety precautions (List B). To be dispensed only on a physician's prescription.

EPILIN PLASTER (Emplastrum epilini)

Epilin is the citrate of p (β diethylaminoethoxy)phenyl phenethyl ketone



White or yellowish fine crystalline powder soluble in water (1:40) and in alcohol. Melting point 118—119°.

Depilatory used in the form of a 4% plaster for removing the hair in treating fungous diseases of the hairy part of the head.

Composition of plaster epilini—4 parts simple lead plaster—51 parts yellow wax—5 parts anhydrous lanolin—20 parts water—20 parts.

The plaster is used according to the following method.

Before applying the plaster the hair is shaved on the affected area, the rest of the hair is clipped short and the head is washed with soap and warm water. The plaster mass is applied in a thin layer to one of the largest foci of infection or to several smaller ones and covered with overlapping strips of sticking plaster or with a gauze dressing and compress paper. The epilatory effect is not confined

to the spot where the plaster is applied but is diffused, for that reason when necessary (for example, when there is acute inflammation at the foci of affection) the plaster can be applied to the healthy areas of the hairy part of the head or to the outer surface of both upper arms or lower legs. When the entire hairy part of the head is involved, it is advisable to apply the plaster to the crown and forehead.

The amount of 4% plaster used depends on the patient's weight, and comes to the following: for a body weight of 10 kg—2 g, 11 kg—2.5 g, 12 kg—3 g, 13 kg—3.5 g, 14 kg—4 g, 15 kg—4.5 g, 16—17 kg—5 g, 18 kg—5.5 g, 19—25 kg—6 g, 26—30 kg—6.5 g, 31—35 kg—7 g, 36—40 kg—7.5 g, 41—50 kg—8 g, over 50 kg—10 g.

Children up to 6 years old are given a single application of plaster which is left on for an average of 20 days. Older children and adults are given two applications, each being left on for 10 days.

If epilation has not taken place by the 20th or 22nd day, or if the effect is insufficient, the plaster is removed and a fresh application made in the same dose. Usually a good epilatory effect follows in 4—6 days. The plaster should not be removed and manual depilation commenced before the 20th day, even when there is a good epilatory effect, early manual epilation before atrophy of the bulb causes breaking of the hair and leads to the early growth of new hair, neither should the plaster be left on the head for more than 25—27 days because of the danger of side effects.

In children of nursery and pre school age, as well as in weak, anemic, undernourished children suffering from heightened nervous excitability, restless sleep and headache, the use of epilator plaster by the "intermittent" method is recommended. According to this method the plaster is left for 3 days in children up to 3 years old, after which the plaster mass is removed and placed in a jar with a ground glass stopper, after an interval of 7—10 days the same plaster is again applied and this time left for 7—8 days.

For children from 3 to 6 years old, the plaster is left on 7 days, after an interval of 7 days a fresh portion of plaster is applied but in half the dose, and left on 7—8 days. For older children, the plaster is also left on 7 days, and a fresh portion applied (full dose) after an interval of 7 days and left on for 7—8 days.

Note. If the plaster used on children up to 3 years old has not been saved a fresh portion is applied in half the dose.

If there should be a marked exacerbation of inflammatory manifestations (suppuration) under the plaster at the focus of affection (for example, in microsporia), the plaster is removed and applied to a healthy area of the hairy part of the head (after shaving).

The hair usually begins to fall out over the entire head by the 12th—14th day after the application of the plaster, first on the temples and gradually spreading being completed on the average by the 20th—25th day.

The plaster is removed when the hair with the atrophied bulbs is easily and painlessly removed in tufts over the entire head when pulled with the fingers.

The entire plaster mass is removed if possible and a pressure dressing of ointment applied, consisting of 2% salicylic acid in petrolatum, and left 24 hrs. Careful manual depilation is then performed. This is followed by the usual iodine ointment treatment for 1½ months, daily painting with 2% tincture of iodine in the morning and application of 10—15% sulfur tar ointment in the evening. The head is washed with soap and brush and manual depilation again performed. The exfoliation method is likewise recommended (to be carried out once or twice), in children up to 6 years old, the salicylic lactic acid ointment should only be used in half the usual concentration, i.e. 6% salicylic and 3% lactic or benzoic acids.

Note. In patients with solitary foci of mycosis the defoliating ointment should not be applied to the entire head but only to the foci of affection.

Tests for fungi are carried out every 10 days.

Patients are to be discharged from the therapeutic institution after two negative results have been obtained in the test for fungi and struck off the register after new healthy hair has grown out over the entire head

Treatment of patients with microsporia should be controlled by means of a luminescent lamp

Before beginning treatment the blood and urine must be examined during treatment these examinations are carried out every 10 days The prescription of ascorbic acid fish liver oil calcium glycerophosphate iron preparations and phytin is recommended

If the use of epilin plaster should be unsuccessful (poor depilation relapse or focal depilation) roentgen depilation is possible after the healthy hair has grown out evenly over the entire head A second application of epilin plaster is not permissible sooner than 3 months after the first and only on condition that there were no complications following the first application In the entire absence of a depilatory effect from the plaster roentgen depilation can be carried out in 3 weeks after the removal of the plaster

Side effects are possible when using epilin plaster follicular hyperkeratosis (chiefly on areas where the plaster is applied at times there is also an eruption of follicular nodules on the cheeks forehead and shoulders) subacute conjunctivitis or blepharoconjunctivitis dryness of the lips Traces of albumin are sometimes discovered in the urine These side effects are quickly eliminated by the usual means

In older children and adults there may be headache and nausea and patients may feel bad these symptoms usually arise on the 9th—10th day after application of the plaster In these cases the plaster should be removed and patients should be prescribed copious fluids and glucose containing ascorbic acid After an interval of 5—7 days epilin plaster can again be applied but in half the dose

In small children (for the most part those with heightened nervous excitement and restless sleep) nightmares sometimes occur on the 4th or 5th day after the application of the plaster (hallucination syndrome) In such cases all the plaster mass should be removed side effects pass away as a rule in 2—3 days Patients should be prescribed copious fluids glucose ascorbic acid phenobarbital and dimedrol

Contraindications infants up to 1 year old diseases of liver kidneys and joints febrile condition gastrointestinal disorders hyperthyroidism constant headache spasmophilia diseases of the nervous system

When preparing the plaster care must be taken to prevent it coming in contact with the skin and mucous membranes or entering the respiratory passages and gastrointestinal tract

To be stored wrapped in cellophane or parchment paper in tightly-closed jars in a cool place observing safety precautions (List B)

ONYCHOLYSIN (Onycholysinum)
A mixture of 15 parts barium sulfide and 85 parts talc. In water onycholysin forms an alkali capable of softening and partially dissolving the keratin of the skin hair and nails

Used for removing the nails in fungous diseases Cold water is added to the powder while stirring until a thick paste is formed this is applied to the nail in a layer up to 0.5 cm thick

A small pit is made in the top of this layer and water added with an eye dropper every 2—3 min so that the pit is always full When the paste is applied carefully to the nail it is not necessary to protect the skin of the nail folds The patient should hold his fingers in a horizontal position so that the drops of water do not flow onto the skin In 30—40 min the onycholysin paste is washed off with water or removed with cotton after which the surface of the nail which has now become a jelly like mass is scraped off with a scalpel (in 15—20 min the nail may again become hard) This procedure is repeated several times until the plate of the nail has been completely removed During the first treatment the entire surface of the nail should be scraped with the exception of the white which is

scraped after the last application of onycholysin. From 1 to 3 applications are necessary for the removal of the nail, depending on its thickness and the degree of affection. Care must be taken when scraping with a sharp scalpel so as not to injure the nail bed.

After the nail has been removed, the patient washes his hands and the nail bed is painted with 10% tincture of iodine.

Onycholysin has no fungicidal properties, for that reason, as soon as the nail has been removed treatment with the following ointment must be commenced: resorcinol, salicylic and lactic (or benzoic) acid — 15 g each, petrolatum — 55 g.

Available in glass jars containing 0.5 and 1 kg.

To be kept in well closed glass containers in a dry place.

L. Phytocide preparations

"Phytoncides" is a name applied to bactericidal, fungicidal and protistocidal substances contained in higher plants (B. P. Tokin). Such substances are contained in considerable amounts in the juices and volatile fractions of the onion, garlic, horse radish and other plants. Preparations obtained from these plants may likewise have an influence on the macroorganism, intensifying the motor and secretory function of the gastrointestinal tract and stimulating cardiac activity.

GARLIC TINCTURE (*Tinctura Allii sativi*)

Mainly used to inhibit processes of putrefaction and fermentation in the intestine in atony of the intestine and colitis, also administered in hypertension and atherosclerosis.

Administered orally, dose for adults — 10–20 drops 2–3 times a day.

Garlic preparations are contraindicated in kidney diseases, since they may cause irritation of the renal parenchyma.

ALLIISAT (*Alliisatum*) 40% alcoholic infusion of garlic bulbs. Administered to adults in a dose of 10–15 drops in milk 2–3 times a day.

ALLILCEP (*Allilcepum*) Alcoholic infusion of onion bulbs (*Allium cepa*)

Light yellow liquid

Administered orally, 15–20 drops 3 times a day for several days in atony of the intestine and diarrhea.

Has likewise been proposed for the treatment of atherosclerosis. Dose 20–30 drops 3 times a day for 3–4 weeks.

ALLILGLYCER (*Allilglycerum*)

Onion preparation, contains phytoncides. Prepared from condensed onion infusion mixed half and half with sterile glycerol. Thick, dark liquid.

Used for the treatment of trichomonadal colpitis. Treatment is to be carried out only on a physician's instructions.

The vagina is cleansed and a sterile gauze tampon 3 cm thick and 20–30 cm long, moistened with allilglycer, introduced. The impregnated tampon should freely fill the vaginal vaults. The length of time the tampon is left in the vagina depends on the sensibility of the patient. It is usually left 6 hrs for the first application, later this time may be increased to 12 hrs. Tampons are applied daily, preferably in the evening.

Irrigation is not performed after the removal of the tampon, but the patient should wash with warm, boiled water. The course of treatment consists in the application of 15–20 tampons.

To be stored in well stoppered vials in a place protected from light.

URSALL (*Ursallum*)

Ethereal infusion of the bulbs and roots of Bear's Garlic (*Allium ursivum*)

Yellow green, slightly turbid liquid with odour of garlic.

Used for the treatment of trichomonadal colpitis, the method is the same as for allilglycer.

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Chapter X

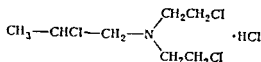
DRUGS USED FOR THE TREATMENT OF NEOPLASMS

I. CHEMOTHERAPEUTIC DRUGS

A. Derivatives of bis-(2-chloroethyl)-amine

NOVEMBICHIN (Novembichinum)

2 Chloropropyl bis (2 chloroethyl) amine hydrochloride



White crystalline substance, freely soluble in water

Novembichin belongs to the group of bis beta chloroethylamines or nitrogen mustard gases

These substances inhibit the multiplication of cells by blocking mitotic division. In the mechanism of this action an important role is played by their alkylating properties and their ability to react readily with nucleic acids, proteins and enzymes. In small doses they readily react with the nucleoproteins of the cell nuclei of the hemopoietic system, as a result of which they inhibit the process of blood formation, the nuclei of hyperplastic (tumour) tissues and lymphoid tissue are also highly sensitive to these substances. Due to their cytostatic action, bis beta chloroethylamines and analogous substances have been proposed for the treatment of tumours of the hemopoietic system, lymph nodes and other organs and tissues.

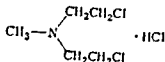
The chloroethylamines are highly toxic, in doses close to the therapeutic they may cause side effects, manifested in pronounced inhibition of hemogenesis by the bone marrow and in impairment of the function of the gastrointestinal tract. When they come in contact with the skin and mucous membranes they have an irritant and vesicant effect, subcutaneous injection of solutions causes necrosis of the tissues. Great caution is necessary when working with drugs of this series.

The first compounds of this group to be proposed for use in medical practice were tri (2 chloroethyl) amine hydrochloride and methyl bis (2-chloroethyl) amine hydrochloride, the latter was given the name Embichin. Synonyms: Caryolsine, Chloramin, Chlorethazine, Chlormethine, Dichloren, Dimutan, Erasin,

Erasol, HN₂, Mechlorethamine hydrochloride, Mustargen, Mustine, Nitrasin
Nitrogranulogen, N Yperit, Stickstofflost



Trichlorotriethylamine



Embiichin

These substances, however, are highly toxic, they often cause vomiting and strongly inhibit hemogenesis by the bone marrow

Novembichin is less toxic than these substances, it inhibits hemogenesis by the bone marrow to a less extent and has a stronger influence on lymphopoesis (L. F. Larionov)

Indications for the use of novembichin I, II and III stage lymphogranulomatosis, chronic lymphadenosis, chronic myeloleukosis, erythremia

Available in sealed ampoules of 10 ml, each containing 10 mg of the dry drug

Administered only intravenously Before use exactly 10 ml sterile Ringer's solution is introduced into the ampoule containing novembichin by means of a 20 ml syringe (it is not advisable to dissolve novembichin in isotonic saline) The solution is at first slightly turbid but becomes transparent in a few minutes. Immediately afterwards the necessary amount of solution is drawn into the same syringe, 1 ml for each mg of the drug required The liquid in the syringe is then diluted to 20 ml with Ringer's solution and injected intravenously

Ringer's solution of the following composition is recommended sodium chloride—9 g potassium chloride—0.42 g, calcium chloride—0.21 g, sodium bicarbonate—0.15 g distilled water to make 1000 ml

Care must be taken to prevent the liquid being injected under the skin If the drug should enter the subcutaneous tissue, some Ringer's solution or isotonic saline should be injected at the spot If the solution should come in contact with the skin or mucous membrane it should at once be washed off carefully with water

Novembichin is administered 3 times a week

Doses should be individualized depending on tolerance and the effect achieved In lymphogranulomatosis, adults are usually given an initial injection of 0.005 g (6 mg) the second injection is 7—8 mg and from then on 9 or less frequently 10 mg The maximal dose for adults is 0.01 g (10 mg) once each second day The single dose for children is 0.07—0.15 mg per kg body weight An indication that the correct dosage has been used is the therapeutic effect achieved, this is manifested in the diminution or disappearance of affected nodes and the abatement of general symptoms (fever, pruritus etc), as well as the slow but continuous decrease in the number of leukocytes in the peripheral blood

The course of treatment usually consists of 12—18 injections

In chronic myeloleukosis injections are begun with 3—4 mg, gradually increasing the dose to 6—10 mg In lymphadenosis, the initial dose for adults is 6 mg followed by 8—9 mg per injection

Treatment with novembichin must be carried out under careful observation by a physician Hematological examinations must be made regularly The therapeutic effect of bis beta chloroethylamines is due to the inhibition of hemogenesis by the bone marrow and to the reduction in the number of leukocytes and platelets, but too pronounced leukopenia and thrombocytopenia are dangerous for the patient It is consequently necessary during treatment to strive to achieve the maximum degree of leukopenia permissible Usually the administration of the drug in lymphogranulomatosis and erythremia is discontinued when the number of leukocytes has fallen to 3000 per mm³ and the number of platelets to 100 000

It must be remembered that the number of leukocytes continues to decrease for some time after the withdrawal of novembichin

In myeloleukosis, injections are continued until the number of leukocytes has fallen to a figure close to the normal, in lymphadenosis, until the number of segmented neutrophils has been reduced to 1500

During treatment with novembichin, as with other derivatives of bis beta chloroethylamine, the transfusion of small amounts of blood as a stimulant (100—125 ml) is recommended. In acute leukopenia transfusions of blood and of leukocyte and thrombocyte mass are given.

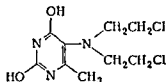
When using novembichin side effects in the form of nausea, vomiting and general weakness are also possible, these symptoms usually appear in 1—3 hrs after injections. They are overcome or abated by the administration of hypnotics (0.3—0.4 g amobarbital sodium orally or 0.5 g in suppositories) or 0.025 g chlorpromazine orally.

Contraindications IV stage lymphogranulomatosis, complete lymphoid metaplasia of the bone marrow, presence of large nodes especially in the abdominal cavity, pronounced anemia, leukopenia and thrombocytopenia, general emaciation, severe affections of liver, kidneys and cardiovascular system, acute leukosis and transition of chronic leukosis to acute, active tuberculosis.

To be kept locked (List A) in sealed ampoules in a place protected from light.

DOPAN (Dopanium)

4 Methyl 5 bis (2 chloroethyl) aminouracil



White crystalline powder, practically insoluble in water, sparingly soluble in alcohol. Melting point 178—179°. Similar to novembichin in chemical structure and influence on the body. Effective when administered by mouth.

Used in the treatment of lymphogranulomatosis, especially in the initial and intermediate stages, and in chronic myeloleukosis in the intermediate and advanced stages (L. F. Larionov and G. N. Platonova).

Dopan can be used in place of novembichin in the treatment of myeloid leukemia, but does not fully replace novembichin in the treatment of lymphogranulomatosis. Dopan is more convenient to use, since it is administered orally; in some cases it is tolerated better, but at the same time it inhibits hemopoiesis by the bone marrow to a greater degree.

Novembichin is superior in the treatment of patients with lymphogranulomatosis who have a low level of hemopoiesis and in the treatment of chronic myeloleukosis.

Doses and length of treatment with dopan should be individualized, depending on the patient's condition, the effectiveness of treatment and the extent to which the drug is tolerated. To be taken at the end of dinner and drunk down with milk, etc.

In the treatment of lymphogranulomatosis dopan is usually administered to adults in a single dose of 0.01 g (10 mg). This dose is given every 5 days (less frequently every 4 or 6 days) 5—7 times in all, depending on the blood picture and the results of treatment. In weakened patients and in cases of heightened sensitivity the dose may be reduced to 0.004—0.006 g (4—6 mg).

The dose for children is calculated at the rate of 0.00015 g (0.15 mg) per kg body weight.

Before each administration of dopan a count of the leukocytes must be made (a count of the platelets is also desirable); treatment is continued until the

number of leukocytes falls to 3000 per mm^3 . It must be borne in mind that the number of leukocytes continues to diminish for some time after dopan is withdrawn.

Another indication for discontinuing the administration of dopan is the fall in the number of platelets to below 100 000.

Something that must be taken into account is that in patients who have received intensive roentgenotherapy the hemopoietic system is more sensitive to dopan. In such patients treatment must be carried out with particular caution. Sometimes smaller doses are used (8 mg) or the drug is given at longer intervals (every 6 days).

In the treatment of myeloleukosis higher doses may be given at the beginning of the course (12 mg). Treatment is discontinued when the number of leukocytes falls to a figure close to normal.

When there is an overdosage of dopan or it is administered too long and also in cases of heightened sensitivity excessive leukopenia may ensue. In order to avoid this complication the precise dosage must be adhered to and close watch must be kept on the patient's condition and the blood picture. It is an advantage to give blood transfusions of 100–125 ml once a week, particularly in patients with a low level of hemopoiesis. In cases of lymphogranulomatosis medicinal stimulants of blood formation such as pentoxyl, sodium nucleate, thesian, etc. should not be used.

If there should be an onset of acute leukopenia, blood transfusions are given 2–3 times a week in the same dose, or leukocyte and thrombocyte mass is administered. Small doses of penicillin may be given to prevent secondary infection. The inhibition of hemopoiesis is usually abolished in 3–4 weeks.

In some patients dopan causes nausea and vomiting in 8–12 hrs after administration. One way of coping with this complication is to give dopan in the evening at the end of supper, followed by a small dose of hypnotic before retiring (0.2 g amobarbital sodium). Another method is to divide the daily dose of the drug into two portions, one being taken in the morning during breakfast, the other after supper. A third method is to administer 25 mg chlorpromazine orally an hour before giving dopan, and again 2–3 hrs afterwards.

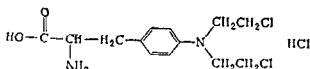
Contraindications: lymphogranulomatosis proceeding with leukopenia (less than 4000 leukocytes per mm^3) and thrombocytopenia (less than 100 000 per mm^3), advanced stage of lymphogranulomatosis accompanied by anemia and emaciation as well as fulminating forms of the disease.

Also contraindicated in severe exacerbations of myeloleukosis (with the appearance of large numbers of hemocytoblasts in the blood) and in acute leukemia. In patients with lymphogranulomatosis who have received roentgenotherapy treatment with dopan should not be commenced before the lapse of 2 months and on condition that the number of leukocytes and platelets in the peripheral blood is normal.

Available in tablets of 0.002 g (2 mg). To be kept locked (List A).

SARCOLYSINE (Sarcolysinum)

d 1 p bis (2-Chloroethyl) aminophenylalanine hydrochloride



Synonym Sarcoclorin

White powder on warming soluble in water (1:15), a precipitate forms when greatly diluted; soluble in dilute acids, alkalis and alcohol.

Sarcosine is a derivative of chloroethylamine and the amino acid, phenylalanine. In chemical structure and general action on the body it is similar to other derivatives of bis beta chloroethylamine.

Used for the treatment of some forms of malignant ulcers: seminoma of the testis (especially if there is metastasis), reticulosarcoma and Ewing's sarcoma. A therapeutic effect has likewise been noted in multiple myeloma, primary cholangiocellular cancer of the liver, tumour of the ovary (complicated by exudation into the abdominal cavity), etc. (L. F. Larionov, A. S. Khokhlov, L. A. Bogomaz and M. M. Belyakova).

In seminoma of the testis with metastasis, treatment with sarcosine is combined with orchiectomy. The drug is not effective in choriomepithelioma and teratoma of the testis.

Administered orally and intravenously.

Available in tablets of 0.01 g (10 mg) for oral administration. For intravenous administration, available in powder form and in sealed ampoules of 20 ml containing 0.01, 0.02, 0.03, 0.04 and 0.05 g.

Solutions are prepared by introducing 10–20 ml isotonic saline into the ampoule, to accelerate solution the ampoule is warmed in water to 60–70°. The effectiveness of treatment is the same when the drug is administered orally or intravenously. Tablets are taken after meals.

The single dose for an adult weighing 60–70 kg is 0.02–0.05 g for adults weighing less than 50 kg and for children the dose is set at 0.0005–0.0007 g (0.5–0.7 mg) per kg body weight. Administered once a week 4–7 doses in all. The drug is usually given in diminishing doses, beginning with 0.04–0.05 g (40–50 mg) per oral administration or injection for adults, and then giving 30–20 mg, and in some cases 10 mg. The dose for the course totals 0.1–0.25 g.

Maximal dose for adults 0.05 g once in 7 days.

Maximal total dose for the course 0.25 g (for adults).

In tumours of the ovaries complicated by exudation into the abdominal cavity, intraabdominal administration of sarcosine is indicated 0.04–0.06 g (40–60 mg) dissolved in 20 ml isotonic saline is administered once a week.

When sarcosine is used, it causes inhibition of hemopoiesis with a decrease in the number of leukocytes, especially neutrophils. During treatment a careful watch must be kept on the blood picture. It must be borne in mind that as in the case of other derivatives of bis beta chloroethylamine, maximum utilization of the therapeutic properties of sarcosine is only possible when there is a certain inhibition of hemopoiesis. Nevertheless, too great a degree of leukopenia, agranulocytosis and thrombocytopenia is impermissible. Administration of sarcosine should be discontinued when the number of leukocytes falls to 3,500 per mm^3 , and also when there is marked thrombocytopenia (below 100,000). At the end of the course of treatment a leukocyte count must be made before every administration of the drug.

After the withdrawal of sarcosine, the number of leukocytes may continue to diminish for another 1–2 weeks. If necessary recourse is had to blood transfusions, 100–125 ml once or twice a week.

In pronounced leukopenia, neutropenia and thrombocytopenia penicillin is administered to prevent the development of infection, and blood transfusions are given, or leukocyte and thrombocyte mass are administered.

If nausea and vomiting should appear during treatment amobarbital sodium is given an hr before the administration of sarcosine (0.5 g in suppositories or 0.3–0.5 g intramuscularly), or 0.025 g chlorpromazine orally.

Contraindicated in the terminal stages of the diseases, cachexia, pronounced anemia, leukopenia (less than 4,000 leukocytes in 1 mm^3) and severe affections of the liver, kidneys and cardiovascular system.

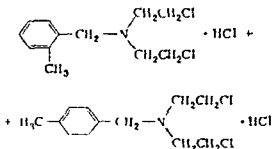
If the patient has previously received roentgenotherapy, sarcosine is not prescribed sooner than 1 month after the end of treatment, in such cases doses of sarcosine are lowered.

If the tumour is sensitive to sarcosine it quickly diminishes in size. If no effect is noted after 2—3 administrations treatment with the drug should be discontinued.

To be kept locked (List A) in well stoppered bottles of amber glass or in sealed ampoules (tablets in hermetically closed vials) in a cool place protected from light.

EMBITOL (Embitolum)

A mixture of *o* and *p* xylyl bis (2 chloroethyl) amine



White crystalline powder, odourless, freely soluble in isotonic saline. Aqueous solutions easily hydrolyze when heated to above 40°.

Similar in action to embichin and novembichin. Embitol is less toxic but is administered in higher doses. When using embitol the same precautions must be observed as when using novembichin.

Used in lymphogranulomatosis (chiefly in limited forms), lymphadenosis (chiefly in subleukemic forms) and lympho and reticulosarcomatosis.

Administered only intravenously. Immediately before use the ampoule is opened (ampoules contain 0.03 g i.e., 30 mg embitol) and 10 ml sterile isotonic saline added by means of a 20 ml syringe. The solution is carefully mixed until the crystals dissolve completely. The necessary amount of 0.3% solution is then drawn into the syringe. Isotonic saline is added to make 20 ml and the solution injected into the vein. Particular care must be taken to prevent the liquid being injected under the skin (see Novembichin p. 419).

Embitol is administered to adults once a day in the following doses: 1st injection — 0.015 g (15 mg = 5 ml 0.3% solution); 2nd injection — 0.02 g (20 mg = 6.5 ml 0.3% solution); 3rd injection — 0.025 g (25 mg = 8.5 ml 0.3% solution). In all cases the 0.3% solution is diluted with isotonic saline to a total volume of 20 ml.

After 3 day treatment a break of one day is made, and then the drug is again administered for 3 days in a dose of 0.03 g (30 mg = 10 ml 0.3% solution). After a one day interval treatment is resumed. Treatment in such cycles is continued until a total of 17—20 injections have been given for the course.

Courses of treatment are repeated if necessary (depending on the clinical and morphological picture) by the same method and in the same doses.

During the course of treatment there must be repeated thorough hematological examinations.

Treatment with embitol can be combined with measures for raising the defensive powers of the body: blood transfusions, vitamin therapy, etc. Other chemotherapeutic drugs having a similar type of action should not be administered simultaneously nor should roentgenotherapy be employed.

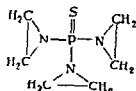
Contraindications and precautionary measures are the same as for novembichin and other bis beta chloroethylamines.

Available in 10 and 20 ml ampoules containing 0.03 g crystalline embitol. To be kept locked (List A) in sealed ampoules.

B Compounds containing ethylene imino groups

THIOPHOSPHAMID (Thiophosphamidum)

Triethylene imide of thiophosphoric acid



Synonyms Thio TEF Thio TEPA TEPA Tespamin Tiofosyl TSPA

White crystalline powder soluble in water and isotonic saline Melting point 52—54° Aqueous solutions are unstable and cannot be sterilized since they are easily hydrolyzed

Thiophosphamid like some other derivatives of ethylene imine has a cytostatic action and inhibits the development of proliferating tissue including malignant tissue An important factor in the mechanism of their action is the impairment of nucleic acid metabolism and blocking of mitotic cell division

Thiophosphamid is used in malignant diseases of the hemopoietic system such as chronic leukosis (chronic myelosis and lymphadenosis) lymphogranulomatosis and lympho and reticularsarcomatosis as well as some forms of tumours cancer of the ovary after non radical operations and in the presence of metastasis presence of metastasis and dissemination in cancer of the mammary gland and cancer of the cervix peritoneal cancer with ascites pleurisy associated with cancer of the lung Thiophosphamid is usually administered intramuscularly and intravenously it can also be instilled into cavities (abdominal and pleural) and injected directly into tumours

Doses and length of treatment should be strictly individualized depending on the character of the disease the patient's general condition the effectiveness of treatment and tolerance to the drug Treatment must be carried out under the careful observation of a physician hematological examinations should be made regularly The drug inhibits blood formation by the bone marrow overdosage or heightened sensitivity may lead to the development of pronounced leukopenia agranulocytosis and thrombocytopenia

Available in vials containing 0.01 and 0.02 g (10 and 20 mg) of the crystalline substance in the form of a tablet Solutions are prepared immediately before use by adding 4 ml of sterile twice distilled water to the vial by means of a syringe

In the treatment of diseases of the hemopoietic system thiophosphamid is administered intramuscularly or intravenously Doses and length of treatment must be individualized depending on effectiveness and tolerance Usually the first few days adults are given 0.01 g daily or each second day and then once in 3—5 days depending on the influence on the number of leukocytes and platelets Subsequent injections are given at intervals of 7—14 days The total dose for the course of treatment comes to 0.1—0.3 g (100—300 mg)

In treating tumours administration of thiophosphamid is begun with higher doses adults are given injections of 0.015—0.02 g each second or third day If there is a slow and moderate decline in the number of leukocytes and platelets this dose is given 3—4 times and then reduced If there is a sharp fall in the number of leukocytes and platelets following the first injections the dose is lowered to 0.01—0.015 g (10—15 mg) and intervals between injections increased to 3—5 days The total dose for the course of treatment averages 0.15—0.2 g If necessary treatment can be repeated after a break of 1½—2 months

If there is exudation into the serous cavities (ascites and pleurisy in tumour of the ovary pleurisy in cancer of the mammary gland etc) intracavity administration of thiophosphamid is indicated The drug is instilled into the abdominal

and pleural cavities in a single dose of 0.02 g (20 mg) in 6–8 ml of isotonic saline after first evacuating the exudate. Instillations are given at intervals of 1–2 days a total of 8–10 administrations (160–200 mg).

During treatment with thiophosphamid a leukocyte count must be made at least each second day and a platelet count at least twice a week. A general blood examination is made once a week.

Administration of thiophosphamid must be discontinued when the number of leukocytes falls to 3000 per mm^3 and the number of platelets to 100 000.

Hematological examinations must be carried out not only during treatment but also for at least 2–3 weeks afterwards since the effect of thiophosphamid on the hemopoietic system persists for some time after it is withdrawn.

During treatment tonic therapy should be carried out including repeated transfusions of small stimulating amounts of blood (100–125 ml) in pronounced leukopenia and thrombopenia transfusions of blood and leukocyte and thrombocyte mass are given in anemia transfusions of erythrocyte mass are given.

If diarrhea should develop — something that is observed in cases of heightened sensitivity to thiophosphamid — the dose is reduced or the interval between injections increased.

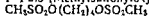
Contraindications: acute leukosis, aleukemic forms of chronic leukosis, general serious condition of patient, cachexia, pronounced leukopenia, thrombopenia and anemia, severe cancerous intoxication, active tuberculosis, hepatitis and nephritis, severe insufficiency of circulation.

To be kept locked (List A) in hermetically closed vials, in a cool place protected from light.

C Esters of disulfonic acids

MYELOSAN (Myelosanum)

1,4-bis (Methylsulfonyloxy) butane



Synonyms: Busulfan, Busulphan, Mielucin, Misulban, Mitostan, Myeleukon, Mylecytan, Myleran, Mysulban, Sulfabutin.

White crystalline powder, insoluble in water. Melting point 116–117°.

The drug has an inhibiting influence on myeloid tissue.

Used for the treatment of chronic myeloid leukemia. Myelosan is less toxic than the derivatives of bis beta-chloroethylamine and is usually tolerated well in therapeutic doses but it should nevertheless also be used with caution since in large doses it inhibits hemogenesis by the bone marrow especially granulocytopenia and thrombocytopenia. If there is heightened sensitivity to myelosan the development of an aplastic (hypoplastic) state of hemopoiesis is possible.

In effective cases the drug causes hematological and clinical remission manifested in normalization of the blood picture, reduction in the size of the spleen and improvement in the general condition.

Administered orally. Doses should be individualized depending on the patient's condition, the effectiveness of treatment and the extent to which the drug is tolerated. In exacerbations of chronic myeloleukosis with moderate splenomegaly and increase in the number of leukocytes to 200 000 per mm^3 , 0.004–0.005 g (4–6 mg) is usually given daily in pronounced splenomegaly with a large increase in the number of leukocytes (over 200 000 per mm^3) initial doses are raised to 8 mg. As the number of leukocytes falls to 100 000–120 000 per mm^3 the dose is reduced to 4 mg. When the number of leukocytes reaches 20 000–30 000 it is reduced to 2 mg. When the number of leukocytes falls to 10 000–15 000 per mm^3 treatment with myelosan must be stopped. When necessary treatment is renewed varying the dose within the range indicated above depending on the course of the disease. During treatment with myelosan an examination of the blood must be made at least every 6 days. During periods of clinical and hematological remission an examination must be made at least twice a month.

Side effects may occur during treatment with myelosan such as vascular dystonia, amenorrhea, pigmentation of the skin and inhibition of the sexual function in males

In cases of inhibition of hemopoiesis transfusions of blood or leukocyte and thrombocyte mass are given

Contraindications: acute and subacute leukosis, exacerbation of chronic myeloleukosis if it proceeds according to the type of acute leukosis, aleukemic and subleukemic forms of chronic leukosis, pronounced thrombocytopenia

Available in tablets of 0.002 g (2 mg)

To be kept locked (List A)

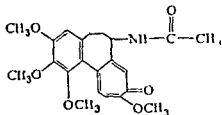
D. Derivatives of colchicine

COLCHAMINE (Colchaminum)

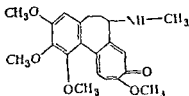
Alkaloid isolated from the corms of the Showy Autumn Crocus (*Colchicum speciosum* Stev.) and the Common Autumn Crocus (*Colchicum autumnale* L.), of the Lily family (Liliaceae)

Synonyms: Omain, Colcemid, Demecolcin

Chemically, colchamine is desacetylmethylcolchicine, i.e., it differs from colchicine in having the N-acetyl group replaced by a methyl radical



Colchicine



Colchamine

Colchamine is similar to colchicine in pharmacological properties but it is only from one seventh to one eighth as toxic

The principal distinguishing characteristic of colchamine is its antimitotic activity. Like colchicine it is a karyoclastic poison and is capable of arresting the development of malignant tissue; it also inhibits leuko- and lymphopoiesis. When applied directly to skin affected with cancer, it causes the breakdown of the malignant cells.

0.5% colchamine ointment (*Unguentum colchamini*) is used as a method for the treatment of cancer of the skin (I and II degree exophytic and endophytic forms). 1–15 g of the ointment is applied to the surface of the tumour and the surrounding tissue to the extent of 0.5–1 cm by means of a spatula and covered with a gauze dressing held in place with sticking plaster. The dressing is changed daily, each time carefully removing the residue of the ointment from the previous application and the broken down cancerous tissue and performing toilet of the surrounding skin. Disintegration of the tumour usually sets in after 10–12 applications. The course of treatment continues 18–25 days; it is only in some cases (in endophytic forms) that it is continued up to 30–35 days. After application of the ointment has been stopped, aseptic dressings are applied for another 10–12 days, thorough toilet of the wound being performed.

Treatment with colchamine ointment is contraindicated in III and IV stage cancer of the skin with metastasis. The ointment should not be applied near mucous membranes as this may lead to toxic symptoms.

Colchamine penetrates through the skin and mucous membranes and in large doses may cause leukopenia, diarrhea, general weakness, elevated temperature and other toxic manifestations.

The ointment must be used with caution more than 1.5 g should not be applied at a time, the blood and urine must be examined regularly

At the first symptoms of a toxic effect, application of the ointment is discontinued, and glucose and ascorbic acid, as well as pentoxyl, thesan or other leukopoietic stimulants administered, blood transfusions are given if necessary.

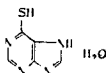
0.5% colchamine ointment is available in jars containing 25, 50 and 100 g
To be kept locked (List A) in closed jars in a cool place

E. Antimetabolites

(Purine antagonists)

MERCAPTOPURINE (Mercaptopurinum)

6 Mercaptopurine



6 Mercaptopurine



Adenine



Hypoxanthine

Synonyms Ismipur, Mercalukin Mercapurene, Purinethol

Slightly yellowish crystalline powder, sparingly soluble in water Melting point 312–314° (with decomposition)

Used in the treatment of acute (subacute) leukosis, and also in exacerbations of chronic myeloleukosis proceeding according to the type of acute leukosis

The antileukemic effect of 6 mercaptopurine is due to its biological action as an antimetabolite of purines 6 Mercaptopurine is closely related, structurally, to adenine (6 aminopurine) and hypoxanthine (6-hydroxypurine) As a structural analogue of these compounds 6 mercaptopurine actively interferes in purine metabolism (see p 66) and disturbs the synthesis of nucleic acids This action is especially marked in some types of tumour cells and in immature leukocytes.

Mercaptopurine is administered orally During the first 3–4 weeks it is given daily in a dose of 0.002–0.0025 g (2–2.5 mg) per kg body weight The daily dose is given at once or is divided for 2–3 administrations Clinical remission often sets in within 1–2 weeks and is manifested in an improvement in the general condition, normalization of temperature, and decrease in the size of the liver and spleen and the peripheral lymph nodes There is a rapid decrease in the number of immature cells in the peripheral blood If there is no clinical effect in 4 weeks from the beginning of treatment and side effects are absent, the dose is gradually raised to 5 mg per kg body weight daily (but no more than that)

Treatment is carried out under careful clinical and hematological control At the first symptoms of a marked decrease in the number of leukocytes in the peripheral blood, treatment is stopped for 2–3 days If there is no further decline in the number of leukocytes, administration of the drug is continued

For greater effect, mercaptopurine is administered in conjunction with hormones (cortisone and ACTH), antibiotics and ascorbic acid, and transfusion of erythrocyte mass

The drug is usually tolerated well but leukopenia, thrombocytopenia, dyspepsy, vomiting and diarrhea may occur In cases of leukopenia, a break is made in treatment, if there are other complications administration of the drug is discontinued Caution must be observed when using the drug in patients with diseases of the liver and kidneys

Available in tablets of 0.5 g

To be kept locked (List A)

II SYMPTOMATIC PREPARATIONS FOR PATIENTS WITH MALIGNANT NEOPLASMS

It is not only specific chemotherapeutic drugs that are used in treating patients with malignant neoplasms but also other medicinal substances of various kinds that influence hemopoiesis metabolism etc.

Among the new agents proposed for improving the general condition of patients with malignant neoplasms are birch fungus preparations and Neocid

BIRCH FUNGUS EXTRACT

Thick extract obtained from the growths formed on birch trees by the phyto pathogenic fungus *Inonotus obliquus*. The preparation also contains a cobalt salt (1% cobalt chloride or 1.15% cobalt sulphate) it is preserved with 10% alcohol

Thick dark brown mass readily soluble in water

Used as a symptomatic agent for improving the subjective feeling of patients with tumours of diverse localization in whom surgical intervention or ray therapy is not indicated. The favourable influence on the general condition may be accompanied by some improvement in the peripheral blood picture. The cobalt contained in the preparation may influence hemopoiesis (see p. 307)

Administered orally in a daily dose of 3.5 g. The extract is usually prepared for administration in the following way: in an amount sufficient for 3 days the vial containing the extract is warmed by immersing it in water heated to 60–70° (after first removing the cork). 2 teaspoonfuls of the extract are diluted with $\frac{3}{4}$ glass of warm boiled water. 1 tablespoonful is taken 3 times a day 30 min before meals.

Also available in tablet form. 1 tablet is taken 4 times a day 30 min before meals.

Treatment can be lengthy: courses of 3–5 months with interval of 7–10 days.

NEOCID (*Neocidum*)

Preparation obtained from the culture medium of a certain microorganism. Dark brown liquid. Faint aromatic odour. Saline acid taste.

According to experimental findings neocid inhibits the development of some forms of tumour in laboratory animals (V. S. Derkach). An improvement in the general condition of cancer patients has been noted after taking neocid.

Neocid does not take the place of surgical ray or chemotherapeutical treatment.

Administered orally and locally.

Administered orally in a dose of 5 ml 3 times a day the first week and 10 ml the next 2 weeks. This cycle of treatment is repeated 2–3 times with an interval of 7 days between.

Applied locally in the form of a lotion (in cancer of the mammary gland) and in the form of a micro enema of 20–50 ml (in cancer of the rectum) as well as for irrigation.

Available in vials. The contents of the vial are thoroughly shaken before use.

To be stored in a cool place protected from light.

Chapter XI

DIAGNOSTIC AGENTS

I. ROENTGENOPAQUE MEDIA

SERGOSIN (Sergosinum)
Sodium iodomethanesulfonate



Synonyms Abrodan Abrodil, Diagnorenol Methiodal natrium, Metiodolum; Neo Sombraven Skiodan sodium, Urombral

White crystalline powder odourless very freely soluble in water (1 2), sparingly soluble in alcohol (1 40), almost insoluble in ether hygroscopic

Aqueous solutions are neutral, they can be sterilized by boiling and are stable if not exposed to light The salt contains about 50% iodine

Used as a radiopaque medium in cystopyelography When injected into the vein it is quickly excreted by the kidneys, filling the pelvis, ureters and bladder, and giving a contrast image in roentgenological examination Also used for testing the secretory function of the kidneys

Administered intravenously in the form of a 40% solution Adults are given a dose of 50 ml i. e., 20 g of the dry salt Dose for children from 8 to 12 years old—15 ml, or 6 g of the dry salt from 12 to 15 years—20 ml, or 8 g of the dry salt

Solutions are prepared immediately before use 20 g powder is dissolved in 50 ml isotonic saline prepared with twice distilled water, the solutions are filtered twice through filter paper and boiled in a water bath 20 min

After cooling the solution to body temperature it is slowly injected into the ulnar vein

Sergosin is rapidly excreted The first roentgenograms are taken in 7—10 min, the second series, in 20—25 min, and the third in 30, 45 or 60 min, by that time not only the contours of the pelvis and ureters are distinctly visible but those of the bladder as well

In ascending (retrograde) pyelography, a 20% solution is introduced into the ureter and pelvis by means of a catheter through a catheterization cystoscope A 10% solution is used for photographing the bladder and urethra

Contraindications heightened sensitivity to iodine, nephritis and nephrosclerosis, active tuberculosis serious diseases of the liver, exophthalmic goiter, decompensated heart disease anuria

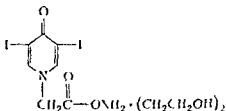
Patients should be warned that there is a disagreeable metallic taste in the mouth immediately after intravenous injections of sergosin At times there is nausea and headache

Available in powder form

To be stored in well stoppered bottles of amber glass

CARDIOTRAST (*Cardiotrastum*)

Diethanolamine salt of 3, 5 diiodo 4 pyridone N acetic acid



Synonyms Abrogen, Arteriodone, Diatrast, Duodone Duodrast Diodon, Diodone, Diodrast, Faltrast, Iopracyl Jodopyracet, Joduron, Jopyracil Leo drast, Neo Methiodal, Neo-Skiodan Neospect, Nosydrast, Nosylan Noviotrast, Nycodrast, Oparenol, Pelviran, Per Abrodil, Perjodal, Per Radiographol, Pyelodrast, Pyelosil, Pyelumbrin, Pyraceton Umbradil Umbragnost, Uriodone, Uro graf, Vasiodone, Viscoiosol, Xumbradil

White crystalline powder, freely soluble in water contains about 50% iodine Aqueous solution colourless, odourless liquid, pH=6.8—7.4

Used as a contrast medium for roentgenological examination of the renal pelvis, ureters and bladder, as well as the blood vessels and heart Also used for testing the function of the kidneys

A 35% solution is used for roentgenological examination of the renal pelvis and ureters, this is warmed to body temperature and slowly injected intravenously (over a period of 3—5 min), keeping careful watch on the patient's condition The dose for adults is usually 20 ml A smaller amount is used for children, depending on the age and weight from 1 to 3 years old — 8 ml, 3—12 years — 8—10 ml, 12—15 years — 10—15 ml

If the kidney function is normal, contrast roentgenograms of the pelvis are obtained in 5 min after administration Usually roentgenograms are taken in 5 15 or 45 min

When there are difficulties in giving intravenous injections, cardiostast is sometimes administered subcutaneously or intramuscularly Preliminary local anesthesia can be used in order to avoid pain When administered subcutaneously, the sterile specified dose (20 ml 35% solution for adults) is diluted with isotonic saline to a total volume of 100 ml 50 ml of the resulting solution is injected subcutaneously in the region of both the right and left scapula Since absorption of the compound is relatively slow when injected subcutaneously, roentgenograms are best taken after a greater lapse of time than when administered intravenously (usually in 30 min)

Intramuscular injections are performed in the gluteal region For adults 10—15 ml 35% solution is injected into each buttock (a total of 30 ml), for children — 5—10 ml into each buttock (a total of 10—20 ml)

For retrograde pyelography, the 35% solution of cardiostast is diluted with sterile isotonic saline to a concentration of 12.5—15% 20 ml of the resulting solution is carefully introduced into the ureters by means of a catheter

For roentgenological examination of the cavities of the heart and the great vessels (angiocardiology), a 50 or 70% solution is used

There are several methods for administering cardiostat for angiocardio-graphy injection into the ulnar, jugular or femoral vein, injection into the heart by means of a sound, through the peripheral veins, or into the aorta through the humeral, radial, carotid or femoral artery.

Usually one of the veins of the elbow flexure of the right or left arm is exposed under local anesthetic and the solution of cardiostat injected. The amount of solution is calculated at the rate of up to 1 ml per kg body weight, but ordi-narily does not exceed 50 ml. The solution is injected rapidly through a needle of large diameter in 1½–2 seconds immediately after the injection (during the first 6–10 sec) 5–6 roentgenograms of the thoracic cage are taken.

Great caution is required when using cardiostat for angiocardiology.

Whatever the method of administration, cardiostat solutions are warmed to body temperature before use. The syringe should be washed with boiled, twice distilled water.

Contraindications: impairment of secretory function of kidneys, liver diseases, active tuberculosis, hyperthyroidism, pronounced debilitation. Cardiostat should likewise be used with extreme caution in cases of marked cyanosis, and in pa-tients with impairment of coronary circulation and myocardial insufficiency.

When using cardiostat, the patient's sensitivity to iodine should be tested in all cases 1–2 days before the examination. For this purpose 1–3 ml 35% cardio-stat solution is injected intravenously. If there are symptoms of iodism (coryza, urticaria, edema) the administration of large doses is dangerous.

When cardiostat is injected there is a sensation of fever and at times ver-tigo, nausea, accelerated pulse and marked cyanosis. Less frequently ptialism, lacrimation and erythematous eruptions occur. Large doses may cause vomiting, considerable lowering of arterial pressure and disturbance of cardiac activity. These symptoms are usually transitory in character. The reaction to adminis-tration can be diminished by the preliminary intravenous injection of 5–8 ml 0.5% procaine hydrochloride solution.

In the case of patients with a past history of allergic reactions, it is advi-sable to give dimedrol or some other antihistamine for several days preceding the administration of cardiostat.

In angiocardiology, besides the side effects arising immediately after the injection of the cardiostat solution, later complications may also occur, throm-bophlebitis at the spot where the sound is introduced and thrombosis of the great vessels.

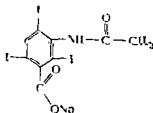
Available in ampoules containing 50 ml 70% solution, 20 ml 35, 50 and 70% solution and 3 ml 35% solution.

Ampoules are to be stored in a cool place protected from light.

During storage of 50 and 70% solutions of cardiostat, partial or complete crystallization of the ampoules is possible. In such cases the ampoule is warmed in hot water to a temperature of 40–45°. If the crystals disappear and the solu-tion becomes completely transparent and no crystals are formed on cooling to 36–38°, the solution is fit for use.

TRIIOSTAT (Triiodostatium)

Sodium 3-acetylamino-2, 4, 6-triodobenzoate



Synonyms Acetrionone Diaginol Iodopaque Jodoren Jodozoal natrium Natrii acetrizoas, Rheopak Sodium acetrizoate Tri Abrodil Triopac Triumbren Urokolon Urokon Urotrast Vesamin

White crystalline powder soluble in water Melting point 260—272° Aqueous solutions are transparent and colourless or slightly yellowish

Used as a contrast medium for roentgenological examination of the renal pelvis ureters and bladder as well as the blood vessels and heart

A 50% solution is used for intravenous pyelography The solution is warmed to body temperature and injected into the ulnar vein over a period of 1—3 minutes The dose for adults is 40 ml that for children 1 ml per kg body weight (up to 12 years old) Nephrograms are taken in 1 min pyelograms in 5—10 min or more

A 30% solution is used for retrograde pyelography For renal angiography 20 ml 70% solution is injected into the abdominal aorta (in 2 sec)

For angiocardiology a 70% solution of triotrast is used in adults and a 50% solution in children The administration technique doses precautionary measures and contraindications are the same as for cardiostast

When using triotrast the patient's sensitivity to iodine must be tested 1—2 days before the examination for this purpose 1—3 ml of 30 or 50% solution is administered intravenously If there are symptoms of iodism triotrast is contra indicated

Available in ampoules or hermetically sealed vials containing 50 ml 70% solution ampoules containing 20 ml 50 and 70% solution 10 ml 30% solution and 3 ml 30 and 50% solution

To be stored in a cool place protected from light

IODOLIPOL (Iodolipolum)

Synonyms Jodatol Jodipin Jodolein Lipiodol

Iodized oil Transparent yellow or brownish yellow only liquid insoluble in water almost insoluble in alcohol Reminiscent of castor oil in odour and taste Miscible with ether and chloroform in all proportions Specific gravity — 1.217—1.227 Contains 29—31% iodine

Used as a contrast medium for roentgenological examination of cavernous organs trachea and bronchi uterus and fallopian tubes (bronchography metro and salpingography)

For bronchography the preparation is introduced through a catheter passed through the nose into the trachea (under roentgenological control) after careful anesthesia of the posterior wall of the pharynx the trachea and the bifurcation of the bronchi 2—5 ml of iodolipol is first introduced gradually adding more to a total of 10—20 ml (more than 20 ml is not used for the examination of one side) For children aged 10—12 years 8 ml is sufficient and for younger children 3—5 ml The patient is placed in the proper position to ensure better filling of the parts of the lung Only one side is examined at a time the second side is not examined before the lapse of 5—6 days When coughing up the iodolipol the patient should not swallow it Food and drink are not allowed before 2—3 hrs after the examination

Contraindications to bronchography with iodolipol general serious condition of patient decompensated heart disease aneurism of the thoracic aorta bilateral diffused pulmonary emphysema acute severely progressing inflammatory processes in the lungs

For metro and salpingography 3—5 ml of the preparation is introduced into the uterus The first roentgenogram is taken immediately after administration the second (for determining the patency of the tubes) in 10—15 min

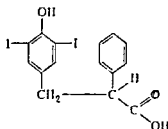
In 15—20 min after introduction the greater part of the preparation is excreted by uterine contraction The preparation remaining in the uterus is absorbed Irritation of the mucous membranes of the tubes and endothelium does not occur

Available in ampoules containing 5 and 10 ml

To be stored in sealed ampoules in a cool place protected from light

IDOALPHIONIC ACID

β (4 Hydroxy 3,5 diiodophenyl) α phenylpropionic acid



Synonyms Bilopsil Biliselectan Bilistram Bilitest Billitrast Bilombrine Bilopsyl Bilospect Choletrast Dikol Teniodol Geatrast Gewagnost Isocole fanine Jodoalphonic acid Jodobil Jodobilan Perfectochol Pheniodol Priodax Sombrabil Tenamid Tenial

White or slightly yellowish light powder faint odour insoluble in water, freely soluble in alcohol Melting point 158—162° Contains about 52% iodine.

Used as a contrast medium for roentgenological examination of the gall bladder and biliary passages (cholecystography) Administered orally in a dose of 3—3.5 g The patient receives a light diet for 1—2 days before the examination at 5 o'clock in the evening the day before the examination he receives supper consisting of 100 g bread 25 g butter and a soft boiled egg At 7 o'clock in the evening he is given a cleansing enema and takes 3—3.5 g bilitrast (1—1.5 g every 20 min) and drinks 3 glasses of sweet tea At 10 o'clock in the evening the patient is given 100 ml 40% glucose solution orally The roentgenogram is taken at 9—10 o'clock the following morning

The following alternative method for using bilitrast is also recommended the first day of preparation the patient is given 20 ml castor oil in the evening and a cleansing enema the second day only light food is permitted At 16 hours he receives 20 g butter and bread and porridge in 2½—3 hrs after his meal the patient takes 3—3.5 g bilitrast and lies on his right side for ½ hr In the evening supper is permitted consisting of a small amount of porridge or mashed vegetables and bread and tea Before retiring he receives 5—7 drops of tincture of opium and a tablespoonful of activated charcoal In the morning 13—15 hrs after taking bilitrast roentgenological examination is performed on an empty stomach if there is no shadow of the gall bladder a second roentgenogram is taken after 3 hrs if there is a shadow the patient is given 2—3 egg yolks in milk and in 1½ hr another roentgenogram is taken

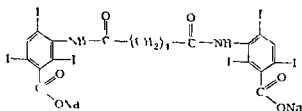
Contraindicated in nephritis uremia and acute gastroenteritis

Available in powder form

To be stored in well stoppered bottles in a dry place protected from light

BILIGNOST (Billignostum)

Sodium salt of N adipyl bis (3 amino 2,4,6 triiodophenyl carbonic acid)



Synonyms Adipiodone, Biligrafin, Cholografin, Cholospect, Endografm, Intrabilix, Iodipamide, Jodipamide, Radioselectan, Sodium iodipamide

White powder, freely soluble in water Contains 64.3% iodine

Used in the form of a 20% solution for roentgenography of the gall bladder and biliary passages The 20% solution is a transparent, yellowish solution, pH=5.5

Administered intravenously The patient's sensitivity to iodine is first tested, for this purpose 1—2 ml 20% solution is injected intravenously the day before If there are no side effects, 30—40 ml are administered, after first warming the solution to body temperature The injection is made slowly — over a period of at least 3—5 min If administered rapidly there may be side effects: nausea, vomiting, a sensation of fever, lowering of the arterial pressure etc

In emergency cases, the patient's sensitivity is determined immediately before the examination 1—2 ml 20% solution is injected intravenously, and if there is no side effect in 2—3 min the necessary amount of the solution (30—40 ml) is administered

In 10—15 min after the injection of bilignost the bile ducts can be detected in the roentgenogram, greater contrast is observed in 25—30 min The gall bladder begins to fill in 40—45 min after administration the maximum intensity of the shadow being observed in 1½—2 hrs In 24 hrs bilignost fills the large intestine, through which it is mostly excreted

Bilignost is used in the following cases: when the gall bladder does not contrast after the administration of radiopaque substances by mouth (bilistrast iodognost), when patients cannot take radiopaque substances orally because of diseases of the gastrointestinal tract, in patients in whom the gall bladder has been removed, when it is necessary quickly to elucidate the condition of the gall bladder and biliary passages

Bilignost is usually tolerated well but in individual cases there may be vertigo, nausea, vomiting and lowering of the arterial pressure These symptoms usually pass away of themselves, if necessary, patients are made to inhale oxygen and given an injection of 1 ml 5% ephedrine solution subcutaneously If the patient has a past history of allergic reactions it is an advantage to administer dimedrol or some other antihistamine for several days before bilignost is used

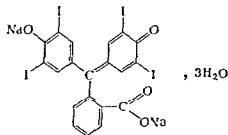
Contraindications obstructive jaundice, acute diseases of liver and kidneys, decompensated heart disease

Available in ampoules containing 10 and 20 ml 20% solution, and ampoules containing 2 ml 20% solution (for sensitivity test)

To be stored in a cool place protected from light

TETRAIODOPHENOLPHTHALEIN SODIUM

Aqueous solution of tetraiodophenolphthalein sodium (about 15%)



Synonyms Antinosine, Biltrast, Bilopac, Cholegnost, Cholotrast, Cholumbral, Cholumbrin Cistopac, Foriod, Iodognost, Jodeikon, Jodikon, Jodophene, Jodophthaleinum natrium, Jodorayoral, Joditragnost, Nosophene sodium, Oral tetragnost, Photobiline, Radiotetrane, Sombrachol, Tethiothalein sodium, Tetraiodophenolphthalein sodium, Tetraiodophthalein sodium, Tetraithalein, Videophiel

Transparent solution dark blue in reflected light, red violet in transmitted light. Contains about 85% Iodine.

Used as a contrast medium for roentgenological examination of the gall bladder and biliary passages (cholecystography).

Careful preparation of the patient is necessary in order to obtain an adequate cholecystogram. After dinner on the first day of preparation the patient is put on a fat free diet for 40 hrs; porridge, fruit and sweet tea are permitted. At 7 or 8 o'clock in the evening on the first day the patient takes the first dose of Iodognost 16—18 ml ($\frac{2}{3}$ of the contents of one vial) in a glass of Borzhomi mineral water or other alkaline water. The solution is drunk in small swallows over a period of 30 min. After taking Iodognost, the patient should lie on his right side for 2 hrs. The next morning the patient takes the second dose of Iodognost, which is given in the same amount and with the observation of the same conditions. The third dose is taken in the evening on the second day (same amount and same conditions). The three doses represent the contents of 2 vials of Iodognost. Cleansing enemas are given after the first dose of Iodognost, in 36 hrs and on the third day, roentgenography is then carried out.

When using Iodognost nausea sometimes occurs and in rare cases vomiting and headache.

Available in vials of amber glass containing 25 ml.

To be stored in tightly closed vials in a place protected from light.

BARIUM SULFATE (Barium sulfuricum, Barli sulfas) BaSO_4

White, loose powder, odourless and tasteless, insoluble in water, dilute acids and alkalis.

Used orally as a contrast medium in roentgenological examination of the stomach and intestine. Prescription should be written out in full "Barium sulfuricum pro Roentgeno" in order to avoid the dispensing of barium sulfide (Barium sulfuratum — BaS) or other soluble barium salts (Barium sulfurosum — BaSO_3 , Barium carbonicum — BaCO_3) which are highly toxic.

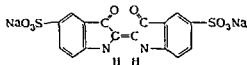
Available in glued, double paper packages (inner layer of parchment paper), containing 100 g.

To be stored unopened in the original packages.

II OTHER DIAGNOSTIC AGENTS

INDIGO CARMINE (Indigocarminum)

Sodium indigotin 5, 5 disulfonate



Dark blue powder, soluble in 100 parts water with the formation of a dark blue solution.

Used for examining the secretory function of the kidneys and the dynamic activity of the renal pelvis and ureters.

The use of indigo carmine is based on the dye's property of being quickly excreted in the urine without impairing the function of the kidneys.

Administered intravenously in the form of a 0.4% aqueous solution. The dose for adults is 4—5 ml; that for children, 2—3 ml. To be injected slowly. The solution is warmed to body temperature before use. When it is impossible to give an intravenous injection 20 ml of the solution is injected intramuscularly.

Excretion of the dye is followed with a cystoscope when unilateral kidney affection is suspected, catheterization of the ureter is performed.

If the function of the kidneys is normal excretion of the dye from the ureters being in 2—3 *min* after intravenous injection imparting a blue colour to the urine. The maximum excretion occurs in 5—8 *min*. In another 3—5 *min* the content of the dye in the urine falls sharply since by then the greater part of the indigo carmine administered has had time to be excreted by the kidneys. excretion is completed in approximately 90 *min*. In cases of impairment of the excretory function of the kidneys, the dye is removed at later periods. excretion is less intensive and more protracted.

Slow excretion of indigo carmine may occur not only in cases of kidney disease but also in patients with decompensated heart disease, hypertensive disease and other diseases accompanied by disturbance of the renal blood flow.

Available in ampoules containing 5 ml 0.4% solution

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(see also *Fmetine*)

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* * *

A

Abicin 148
 Acetaminophenol 60
 Acetarsonc 378
 Acetazine 23
 Acetazolamide 183
 Acetonchloroform 17
 Acetophen 60
 Acetylcholine chloride 87
 Acidin pepsin 283
 Acidol pepsin 283
 Acriflavine 410
 Adenosine triphosphate 299
 — — disodium salt 300
 — — monocalcium salt 300
 ACTH 253
 ACTH zinc phosphate 256
 Adalin 19
 Adiurecrin 257
 Adonis 150
 — extract 150
 — brom 150
 Adonisid 150
 Adrenalin 114
 Adrenocorticotrophic hormone 253
 Aeron 101
 Albichthol 407
 — paste 407
 Albomycin 317
 Albucid 346
 — sodium 347
 Albumin tannate 205
 Allacil 185
 Alliecep 418
 Alliglycer 418
 Allisat 418
 Allochol 223
 Aloe emulsion 309
 — extract 309
 Althea root 215
 — dry extract 215

Alum, aluminum potassium 209
 — burnt 209
 Aminarsone 269
 Aminazine 25
 Aminoacrichin 391
 Aminochinol 373
 Aminopectid 289
 Aminophylline 171
 Aminopyrine 55
 Aminotartrate phosphate 166
 Amital sodium 11
 Amizyl 36
 Ammonium chloride 183
 Amobarbital sodium 11
 Amyl nitrite 164
 Analgesic emulsion 54
 Analgin 56
 Anesthesia 196
 Angiotrophin 179
 Antabus 314
 Antasthman 171
 Antianemin 236
 Antiasthmocrin 116
 Antidiuretic hormone 257
 Antiformin 400
 Antipsoriaticum 212
 Antipyrine 54
 Anti smoke mixture 3, 4
 Antistrumin 304
 Antorphone 50
 Anusol 100
 Apigenin 207
 Apocynum cannabinum 151
 Apomorphine hydrochloride 214
 Apressine 122
 Aprophen 173
 Aralia tincture 80
 Armine 95
 Arnica flowers 253
 — tincture 253
 Arsenic acid anhydride 303
 Arsenic pentoxide 303

Arsenic white 303
 Arsenical tablets 303
 Ascaridol 387
 Ascorbic acid 237
 Ascophen 53
 Asphen 53
 Aspirin 52
 Asthma powder 100
 Asthmatin 102
 Asthmatol 100
Asragalus downy flowered 78
 Atophan 296
 ATP 299
 Atropine 97
 Aureomycin 333
 Avtol ointment 410
Axerophthol 225
 Azamethonium bromide 109
 Azulene 207

B

Bactericidal paper 405
 Baikal Skullcap rhizome 178
 BAL 310
 Balsam Sanitas 54
 — Shostakovsky's 409
Barbamyi 11
 Barberry, Amur 195
 — European 195
 Barbitol 8
 Barbitol sodium 9
 Barbituric acid 6
 Barium sulfate 436
Barofal 12
 Baum Bengue 54
 Bearberry leaf 189
 Becarbon 100
 Bekhterev tablets 22
Belladonna preparations 99
 — extract 99
 — leaf 99
 — root juice 100
 — tincture 99
 Benzacin 105
Benzamon 90
 Benzoehexony 107
 Benzoic acid 402
 Benzonaphthol 408
 Benzylchlorpropionamide 68
 Benzylpenicillin 327
 — procain 331
 Bepasc 358
 Besalol 100
 Belasin 282
 Bethiol 100
 Betony 195

Bicarmint 402
 Bicillin 331
 Bigumal 362
 Buochinol 380
 Bilignost 434
 Bilitrast 434
 Biomycin hydrochloride 333
Birch buds 189
 — leaf 189
 — fungus extract 429
Bismoxerol 380
 Bismuth nitrate, basic 207
 — subgallate 208
 — subnitrate 207
 — tribromophenate 208
 — — ointment 208
Bistort rhizome 206
 Bithiuril 381
 Bitter tincture 212
 Bland's arsenic tablets 303
 — tablets (dragees) 307
 Boromenthol 209
Brilliant green 413
 Bromisovalum 19
 Bromural 19
 Buck Bean leaf 213
 Buckthorn bark 219
 — — dry extract 219
 — — fluid extract 219
Burdock root 189
Burnet rhizome and root 206
 Butadion 58
 Butamid 261

C

Caffeine 67
 — sodium benzoate 68
 Calcex tablets 406
Calciferol 241
Calcium aurothiopropanolsulfonate 362
 — carbonate, precipitated 295
 — chloride crystalline 297
 — gluconate 298
 — glutamate 285
 — glycerophosphate 301
 — iodobehenate 304
 — lactate 299
Calendula nicotinic acid tablets 231
Calomel 221
 Camphor 68
 — bromated 69
 — ointment 69
 — powdered 69
 Camphorated oil 69
 Campolon 236
 Capsicum compound liniment 210
 — tincture 210

Capsin 51
 Carbacholine 89
 Carbarsone 369
 Carbocholine 89
 Carbolen 201
 Carbromal 19
 Cardiotrast 431
 Cardiovalen 157
 Carlsbad salt artificial 220
 Catechins 239
 Celanide 147
 Cement BF 6 410
 Centaury herb 213
 Chamomile flowers wild 207
 Charcoal activated 204
 — — tablets 204
 Chenopodium oil 387
 Chimiofon 321
 Chinocid 366
 Chloracon 68
 Chloralhydrate 17
 Chloramphenicol 318
 Chloretone 18
 Chloridin 364
 Chlorguanide hydrochloride 362
 Chlorobutanol 17
 Chloroform water 4
 Chlorothiazide 186
 Chlorpromazine 25
 Chloritetracycline hydrochloride 333
 Cholenzym 223
 Choline chloride 237
 Chologon 222
 Cholasas 223
 Chorionic gonadotropin 278
 Chrysanol 362
 Cimicifuga tincture 178
 Cincophen 296
 Cinquefoil rhizome 207
 Citral 227
 Citramon 53
 Clay white 203
 CN tablets 231
 Coamid 307
 Codeine 43
 — phosphate 44
 Codterp n 44
 Coffecristine 191
 Coffetamine 191
 Colchamine 427
 — ointment 427
 Colimycin 338
 Collargol 404
 Colloidal silver 404
 Colts foot leaf 218
 Common hops 39
 Condelphine 129
 Contraceptin 414

Convallatoxin 153
 Convasid 151
 Corazol 69
 Corbella tablets 100
 Cordiamine 71
 Cordigit 145
 Corelborin 161
 Coresid 156
 Corglycon 155
 Cornflower flowers 189
 Corrosive sublimate 402
 Cortisone 58
 Colamine chloride 193
 Cranberrybush bark 253
 — — fluid extract 253
 Crystal violet 389
 Curare 121
 Cutizone 397
 Cyclochin 367
 Cyclodol 66
 Cygerol 409
 Cymarin 157
 Cyliton 85

D

Dandelion root 213
 — thick extract 213
 Daucarin 177
 Decholin 223
 Dihydrocholic acid 222
 Delsemine 128
 Dermatol 208
 Desacetyldigilanide 146
 Deschlorbiomycin 337
 Descurinia Sophia 222
 Deserpidine 33
 Desoxyephedrin 73
 Dextran 291
 Dextromoramide 49
 Diacarb 183
 Diazolin 137
 Dibazol 176
 Dicain 200
 Dicolin 110
 Diethazine 65
 Diethylstilbestrol 267
 — dipropionate 267
 Digalen neo 148
 Digicil 149
 Digicilen 149
 Digilanide A 146
 Digipuren 145
 Digitalin 143
 Digitalis extract 143
 Digitaliside 145
 Digitoxin 143

Digoxin 146
 Dihydrochlorothiazide 187
 Dihydrocodeinone 44
 Dihydrostreptomycin 326
 — PAS 327
 Diiodotyrosine 281
 Dilanide 147
 Dilantin sodium 61
 Dimedrol 133
 Dimercaptopropanol 310
 Dimerine 14
 Dimestrol 269
 Dinezin 65
 Diocid 403
 Dionin 46
 Diphacyl 104
 Diphenine 61
 Diphenylhydantoin sodium 61
 Diplocaine 126
 Diprazin 135
 Diprophene 174
 Diprophylline 172
 Disulfiram 351
 Ditilin 130
 Ditrazine 387
 Diuretin 169
 Dopan 421
 Duotal 214
 Duplex 302
 Dustundan 414

E

Echinopanax tincture 79
 Echinopsine 83
 Ecmolin 339
 Ecmovocillin 331
 EDTA 312
 Elatine 128
 Elder flowers 207
 Embitol 424
 Emetine hydrochloride 370
 Endoxycin 308
 Ephedrine 118
 Epilin plaster 415
 Ergocalciferol 241
 Ergometrine maleate 192
 Ergot 190
 — fluid extract 192
 — powder 191
 Ergotal 192
 Ergotamine tartrate 193
 Ergotoxine 121 190
 Erysimin 156
 Erythromycin 333
 Escodol 48
 Eserine 90
 Estradiol dipropionate 265

— — monobenzoate 264
 Estrone 263
 Etapyrazine 24
 Ethacridine 411
 Ethaminal sodium 12
 Ethazole 348
 — sodium 349
 — soluble 349
 Ether 3
 —, anesthetic 3
 — medicinal 3
 Ethereal extract 389
 Ethoxyd 360
 Ethyl aminobenzoate 195
 — — suppositories 197
 Ethyl chloride 5
 Ethylenediaminetetraacetic acid disodium salt 312
 — calcium disodium salt 311
 Ethylmorphine hydrochloride 46
 Etisine 136
 Eucalyptus leaf 210
 — tincture 210
 Eucommia bark 178
 Eulevomycetin 320
 Euphyllin 171
 Eusynthomycin 322
 Everlasting flowers 223
 — — dry extract 223
 Eye ointment 403

F

Fenethazine 136
 Fern male 389
 Ferrogemagen 305
 Ferrous carbonate, with sugar 306
 Ferrous sulphate 307
 FIBs 309
 Filixan 391
 Flamin 223
 Flavacridine hydrochloride 410
 Flax Weed seed fluid extract 222
 Folic acid 233
 Folliculin 263
 Fowler's solution 302
 Foxglove, ciliated 149
 —, purple 141
 —, rusty 148
 —, wooly 145
 Frostbite ointment 211
 Furacin 394
 Furadonine 395

G

Galanthamine 93
 Gallotannic acid 205

Gangleron 175
 Garlic tincture 418
 Gastric juice, natural 283
 — —, artificial 283
 Gendon 31, 34
 Gentian root 212
 — — thick extract 213
 — — tincture 213
 Gentian violet 389
 Gentiana lutea 212
 Ginseng root 79
 Gitalin 141
 Gitalin 145
 Gitalin 141
 Glauber's salt 220
 Glucose 294
 Glutamic acid 285
 Glycerophosphate, granules 301
 Glycerophosphen 301
 Gnaphalium bog 178
 Gramicidin S 397
 Gramicidin contraceptive paste 398
 Grape sugar 294
 Guaiacol carbonate 216

H

Halazone 400
 Haws 162
 Hellebore black 160
 — Caucasian 160
 — false 150
 Hematogen 308
 — children's 308
 Hemostimulin 306
 Henbane leaf 102
 — — extract 103
 — oil 103
 Heparin 248
 Hesperidin 239
 Hexabenzal 107
 Hexachloroethane 392
 Hexamidin 62
 Hexenal 14
 Hexestrol 265
 Hexobarbital sodium 14
 Hexonium 107
 — B 107
 Hips, rose 239
 Histamine 132
 Histidine 287
 Homatropine hydrobromide 102
 Hops, common 39
 Horsetail herb 189
 Hyaloid body 307
 Hyaluronidase 283
 Hydrocodone 44
 — phosphate 44

Hydrolysate, protein 289
 Hydrolysin 268
 Hydropertit 401
 Hydropiperin 253
 Hydroxyquinoline 413
 Hydroxytetracyclin 336
 Hyoscine hydrobromide 101
 Hyoscyamus niger 102
 Hypersol 297

I

Ichthammol 407
 — nallalan petroleum paste 407
 — ointment 407
 — suppositories 407
 Ichthiol 407
 Imanin 399
 Imerellin Buckthorn 219
 — — decoction 219
 — — fluid extract 220
 Imizin 77
 Indigo carmine 436
 Ingacamph 210
 Ingaphen 73
 Insulin 259
 — zinc suspension 260
 Intermedin 256
 Inula helenium 218
 — rhizome and root 218
 Iod hypersol 301
 Iodoaliphonic acid 431
 Iodoform 401
 Iodognost 435
 Iodolipol 433
 Iprazid 76
 Iron lactate 306
 —, reduced 305
 Isadrin 119
 Isaphenin 221
 Isolanid 148
 Isoniazid 352
 Isoprime 113
 Isoverine 194

J

Jacob's Ladder rhizome and root 216
 Juglone 361
 Juniper fruit 188
 Jute Potsherb 158

K

Kallikrein 179
 Kalypnon 12
 Kaolin 203
 Karmanova tablets 10

Khellin 176

L

Lagochilus 252
Laminaria 222
Lantoside 146
Larusan 357
Laughing gas 5
Lead acetate 208
— plaster simple 405
Lecithin 301
Lecithin cerebro 301
Ledum palustre 217
Leonurus 39
— tincture 39
Leucine 287
Leucogen 247
Leuzea 79
Levant Wormseed 384
Levomycetin 318
Licorice root 217
— — dry extract 217
Lidol 46
Lily of the Valley 153
— drops 153
— extract 153
— herb 153
— tincture 153
Lime flowers 179
Linol 245
Lipocain 262
Lipocerebrin 301
Liver extract 236
Lobeline 83
Luminal 9
Luronit 307
Lydasa 283
Lysergic acid 191
— — diethylamide 191
Lysoform 406
Lytic mixtures 27

M

Magnesia white 295
Magnesium carbonate basic 295
— glutamate 287
— oxide 295
— sulphate 37
— trisilicate 204
Magnolia Southern 178
Maize silk 224
Male Fern 389
Mammophysin 258
MAP 300
Medinal 9
Mellicline 129

Menthyl valerate 210
Menyanthes trifoliata 213
Mepanit 106
Mepazine 29
Mephenesin 35
Meprofan 34
Mercamin hydrochloride 313
— salicylate 314
Mercaptopurine 428
Mercazolil 280
Mercuric bimodide 383
— chloride 402
— — ammoniated 403
— cyanide 382
— ointment grey 382
— oxide yellow 403
— oxycyanide 403
— salicylate 382
Mercurous chloride 221
Mercury bichloride 402
— ointment grey 382
Mercusal 180
Meridil 75
Mesaton 117
Mesocain 201
Metazid 356
Methacin 106
Methenamine 406
Methoxy diethylaminopropylaminoqu
noline 365
Methylandrostandiol 277
Methylene blue 412
Methyl salicylate 54
Methylsulfazine 345
Methyltestosterone 275
Methylthiouracil 279
Methyl violet 389
Methypylon 14
Microcid 398
Monobromated camphor 22
Morphine 41
Mother of Thyme herb 217
Motherwort 39
— tincture 39
Muscle Adenylic preparation 300
Myanesin 35
Myarsenol 377
Mycerin 339
Myelosan 426

N

Naftalan 409
— emulsion 409
— petroleum refined 408
Nalorphine 50
Nanophyn 114
Naphthyzin 120

Narcolan 20
 Neobenzoinol 212
 Neocid 429
 Neodicoumarin 250
 Neriolin 160
 Nettle leaf 252
 Nicotinamide 230
 Nicotinic acid 230
 Nikethamide 71
 Nitranol 166
 Nitrofurantoin 395
 Nitrofurazone 394
 Nitroglycerol 165
 — solution 165
 — tablets 165
 Nitrous oxide 5
 Nivalin 93
 Noradrenalin 116
 Norsulfazol 343
 — soluble 344
 Novarsenol 375
 Novembichin 419
 Novikov's antiseptic liquid 413
 Novocain 197
 Novocainamide 161
 Novocephalin 53
 Novomigrophen 56
 Nutgalls 205
 Nux Vomica 82
 — — dry extract 82
 — — tincture 82
 Nystatin 339

O

Oak bark 206
 Octestrol 270
 Ointment avtol 410
 — bismuth tribromophenate 208
 — colchamine 427
 — eye 403
 — frostbite 211
 — mercuric grey 382
 — — yellow 403
 — Naftalan petroleum 408
 — undecin 414
 Oleander 159
 Oleandrin 160
 Oltoriside 158
 Omain 427
 Omelen 178
 Omnopon 42
 Onycholysin 417
 Opium 39
 — dry extract 40
 — powdered 40
 — tincture, simple 40
 — tincture benzoated 41

Osarbon 379
 Osarcid 379
 Osarsol 378
 Oxycodone hydrochloride 45
 Oxytetracyclin 336
 Oxytocin 257

P

Pachicarpine 112
 Padutin 179
 Palfium 49
 Pancreatin 282
 Pantocid 400
 Pantocrin 60
 Papaverine hydrochloride 166
 Paraldehyde 18
 Paramyon 127
 Parathyroidin 259
 Passiflora incarnata 39
 Passion Flower, incarnate 39
 Pectol 41
 Pectussin 209
 Pelodistillate 309
 Peloidin 309
 Penicillin 327
 — V 332
 Pentabismol 381
 Pentamin 109
 Pentobarbital sodium 12
 Pentoxyl 216
 Pentyleneetetrazol 69
 Peppermint leaf 208
 Pepsin 282
 Periplocin 159
 Pertussin 217
 Pervitin 73
 Phenacetin 59
 Phenadone 48
 Phenamine 72
 Phenatine 74
 Phenobarbital 9
 Phenolphthalein 220
 — tablets 221
 Phenoxymethylpenicillin 332
 Phenylin 251
 Phosphacol 94
 Phosphren 301
 Phthalazol 349
 Phthivazid 353
 Physostigmine 89
 Phytin 300
 Phytoferrolactol 301
 Pine buds 218
 Piperazine 385
 — adipinate 385
 — citrate 386
 — hexahydrate 385

- phosphate 386
- sulphate 385
- Pyridrol 75
- Pituitary extract 257
- Pituitrin 257
- Plantain leaf 217
- juice 217
- Plasmocid 365
- Plasmol 308
- Platyphylline 103
- Polygala root 215
- Polyglucin 291
- Polygonum carneum rhizome 206
- Polymerol 410
- Polymyxin M, sulphate 398
- Polyvinylbutyl ether 409
- Polyvinylpyrrolidone 292
- Pomegranate bark 392
- Potassium arsenite, solution 302
- iodide 303
- — tablets 304
- perchlorate 280
- permanganate 401
- Potentilla erecta 207
- Pregnantol 194
- Pregnin 272
- Procainamide 161
- Procaine base 199
- hydrochloride 197
- Progesterone 271
- Prolactin 256
- Promazine 28
- Promedol 46
- Promeran 182
- Promethazine 135
- Propazine 28
- Proserine 91
- Protamine sulphate 250
- zinc insulin 260
- Protargol 404
- Protein hydrolysate 289
- Psoriasis 211
- Purgen 221
- Pyramein 56
- Pyramidon 55
- Pyraminal 56
- Pyraphen 56
- Pyridoxine 231
- Pyrimethamine 364
- Pyrophos 96

Q

Quetel 13

R

Rastinon 261
Rauwolfia 30

Rescinamine 33
Reserpine 31
Resorcin 407
Resorcinol 407
Rest harrow 222
Retinol 225
Rhubarb 218

- bitter alcoholic tincture 219
- dry extract 219
- powder 219

Riboflavin 229
Ringer — Lock solution 294

- tablets

Romidasa 284
Rose hips 239
Rutamin 240
Rutin 240

S

Sage leaf 207
Saiodin 304
Salicylamide 53
Salicylic acid 402
Salmiment 54
Salol 408
Salsolidine hydrochloride 168
Salsoline hydrochloride 167
Salts bitter 37

- , Epsom 37
- , Glauber's 220

Saluzid 355

- , soluble 355

Sanazin 374
Santonica 384
Santonin 383
Sarcocolline 422
Saturant 149
Schizandra 79

- fruit and seeds 78

Scophedal 48
Scopolamine hydrobromide 100
Sea Buckthorn oil 243
Secadol 191
Securinine 82
Senecio 103
Sergosin 430
Serum therapeutic (LSB) 289

- , BK 8 290

Shostakovsky's Balsam 409
Silk vine 159
Silver, colloidal 404
Silver protein 404
Shepherd's Purse herb 195

- — — dry extract 195

Soaproot 218
Sodium antimonyl tartrate 303

- arsenate 302

- benzoate 216
- chloride 293
- citrate 251
- decholate 223
- hypochlorite alkaline 400
- iodide 301
- nitrite 164
- nucleinate 246
- para aminosalicylate 357
- salicylate 51
- sulphate 220
- thiosulphate 311
- usnate 399
- Solusulfone 395
- Solusurmin 368
- Solution Fowler's 302
- Ringer — Lock 294
- Sorbex 207
- Sovcain 203
- Spasmolytin 101
- Sphaerophysine 113
- Spirit of camphor 69
- Splenin 308
- Spurred rye 190
- Sterculia tincture 80
- St John's wort herb 206
- Stomach tablets 101
- Streptocid 341
- soluble 342
- Streptomycin calcium chloride, com
plex 325
- Streptomycin sulphate 322
- Strophanthin 151
- Strophantus tincture 153
- Strychnine nitrate 81
- Stypticin 193
- Styptic pencils 209
- Succidifer 149
- Sucradbel 100
- Sugar of lead 208
- Sulfacetamide 346
- , soluble 347
- Sulfacyl 346
- Sulfadimezine 345
- Sulfamethin 360
- Sulfanilamide 341
- emulsion 342
- ointment 342
- suspension 342
- Sulfanilamide soluble 342
- Sulfazine 344
- Sulfodiamine 396
- Sulfodimezine 345
- Sulfonin 360
- Sulgin 350
- Sygethin 270
- Synestrol 266

Synthomycin 321
— emulsion 321

T

Talc 204
Tannalbin 205
Tannin 205
Tansal 205
Terpin hydrate 215
Terramycin 336
Testosterone enanthate 275
— propionate 273
Telamon 111
Tetracyclin 337
Tetraiodophenolphthalein sodium 435
Telridine 13
Teluram 314
Thallium plaster 414
Thealbin 206
Thecodine 45
Theobromine 169
— sodium salicylate 169
Theophedrine 171
Theophylline 170
Thermopsis herb 215
— — dry extract 215
Thesan 247
Thiamine hydrobromide 227
— hydrochloride 229
Thiodiphenylamine 22
Thiopental sodium 16
Thiophosphamid 425
Thio TEF 425
Thorn apple leaf 102
Thyreoidin 258
Tibon 359
Tiphen 173
Toxiferine 123
Triacanthine hydrochloride 176
Tribromoethanol 20
Trichloromethane 4
Trichlorotriethylamine 420
Trichomonacid 372
Triiodomethane 401
Trioltrast 432
Trimecain 201
Trimethine 64
Tripazol tablets 411
Tropacin 64
Trypallavine 410
TsOLIPK protein hydrolysate 289
Tubazid 352
Tubocurarine 124

U

Undecin 414
— ointment 414

Unithiol 310
Urodan 296
Urosulfan 348
Urotropine 406
Urozin 296
Ursall 418

V

Valerian rhizome and roots 38
— *etheral tincture* 39
— *extract* 39
— *infusion* 38
— *tincture* 38
Validol 210
Verodon 56
Veronal 8
— *sodium* 9
Vicalin 208
Vikasol 245
Vinylin 409
Vitamin A 225
— — *oil solution* 226
— B₁ 227
— B₂ 229
— B₆ 231
— B₁₂ 233
— B_c 233
— C 237
— D 241
— E 242
— K 244

— P 239
— PP 230

W

Water Pepper herb 252
— — — *fluid extract* 253
Wild Marjoram herb 217
Wild Rosemary herb 217
Wormwood herb 213
— — *thick extract* 213
— — *tincture* 213

X

Xanthine 66
Xeroform 208
— *ointment* 208
Xycain 202

Y

Yarrow herb 252
Yatren 371

Z

Zinc sulfate 405
Zincundan 414

CONTENTS

Page

Chapter I

MEDICINAL AGENTS ACTING PREEMINENTLY ON THE CENTRAL NERVOUS SYSTEM

I Anesthetics and hypnotics	3
<i>A Agents for inhalation anesthesia</i>	3
Ether	3
Chloroform	4
Ethyl chloride	5
Nitrous oxide	5
<i>B Hypnotics and anesthetics derived from barbituric acid and other heterocyclic compounds</i>	6
a) Hypnotics of the barbituric series	8
Barbital	8
Barbital sodium	9
Phenobarbital	9
Amobarbital sodium	11
Pentobarbital sodium	12
Barotal	12
Quietal	13
b) Hypnotics derived from pyridine and piperidine	13
Telidine	13
Methypylon	14
c) Barbiturates used for intravenous anesthesia	14
Hexobarbital sodium	14
Thiopental sodium	16
<i>C Hypnotics and anesthetics of the aliphatic series</i>	17
Chloralhydrate	17
Chlorobutanol	17
Paraldehyde	18

Carbromal	19
Bromisovalum	19
Tribromoethanol	20
II Sedatives and neuroplegic agents	21
<i>A Bromides</i>	22
Monobromated camphor	22
<i>B Phenothiazine derivatives</i>	22
Chlorpromazine	25
Promazine	28
Mepazine	29
<i>C Rauwolfia alkaloids</i>	30
Rauwolfia	30
Reserpine	31
Deserpidine rescinnamine and other Rauwolfia drugs	33
<i>D Derivatives of propanediol and diphenylmethane</i>	34
Meprotan	34
Amizyl	36
<i>E Miscellaneous sedatives</i>	37
Magnesium sulphate	37
Valerian	38
Motherwort	39
Incarnate Passion flower	39
Common hops	39
III Analgetics, febrifuges and antiphlogistics	39
<i>A Analgetics of the opium group and their synthetic substitutes</i>	39
Opium	39
Morphine	41
Omnopon	42
Codeine	43
Codeine phosphate	44
Hydrocodon	44
Oxycodone hydrochloride	45
Ethylmorphine hydrochloride	46
Promedol	46
Phenadone	48
Dextromoramide	49
<i>B Antagonists of morphine and other analgetics</i>	50
Antorphone	50
<i>C Analgetics, febrifuges and antiphlogistics — derivatives of salicylic acid pyrazolone and aniline</i>	51
<i>a) Derivatives of salicylic acid</i>	51
Sodium salicylate	51
Aspirin	52
Salicylamide	53
Methyl salicylate	54

b) Derivatives of pyrazolone	51
Antipyrine	54
Aminopyrine	55
Analgin	56
Butadion	58
c) Derivatives of aniline	59
Phenacetin	59
Acetaminophenol	60
IV Anticonvulsants	60
<i>A Substances used in the treatment of epilepsy</i>	61
Diphenylhydantoin sodium	61
Hexamidin	62
Benzylchlorpropionamide	63
Trimethine	64
<i>B Substances used for the treatment of parkinsonism</i>	64
Tropacin	64
Diethazine	65
Cyclodol	66
V Agents stimulating the central nervous system	66
a) Derivatives of purine	66
Caffeine	67
Caffeine sodium benzoate	68
b) Drugs of the camphor pentylenetetrazol and nikethamide group	68
Camphor	68
Pentylenetetrazol	69
Nikethamide	71
c) Drugs of the phenamine group (phenyl alkylamines)	72
Phenamine	72
Desoxyephedrin	73
Phenatine	74
d) Derivatives of diphenylmethane	75
Piridrol	75
Meridil	75
e) Hydrazines	76
Ipiazid	76
f) Derivatives of iminodibenzyl	77
Imizin	77
g) Plant extracts and animal tissue preparations which have a stimulating effect on the central nervous system	78
Schizandra fruit and seeds	78
Ginseng root	79
Leuzea	79

Sterculia tincture	80
Aralia tincture	80
Panlocrin	80
h) Drugs of the strychnine group	81
Strychnine	81
Securinine	82
Echinopsine	83
i) Respiratory stimulants	83
Lobeline	83
Cylton	85

Chapter II

~ MEDICINAL AGENTS ACTING PREEMINENTLY IN THE REGION OF THE ENDINGS OF THE EFFERENT (CENTRIFUGAL) NERVES

<i>I Substances acting preeminently on organs innervated with autonomic nerves</i>	87
<i>A Acetylcholine and cholinomimetic substances</i>	87
Acetylcholine chloride	87
Carbocholine carbacholine	89
Benzamon	90
<i>B Anticholinesterase agents</i>	90
Physostigmine, eserine	90
Proserine	91
Galanthamine	93
Phosphacol	94
Armine	95
Pyrophos	96
<i>C Cholinolytic agents acting preeminently in the region of the peripheral cholinoreactive systems</i>	96
<i>a) Substances of natural origin (alkaloids of the atropine and platyphylline group and plants containing them)</i>	97
Atropine	97
Belladonna preparations	99
Scopolamine hydrobromide	101
Homatropine hydrobromide	102
Thorn apple leaf	102
Henbane leaf	102
Platyphylline	103
<i>b) Synthetic substances (esters of carbonic acids)</i>	104
Spasmolytin	104
Benzacin	105
Methacin	106
Mepant	106
<i>D Ganglion blocking agents</i>	107
Benzohehexony	107
Azamethonium bromide	109

Dicolin	110
Telamon	111
Pachycarpine	112
Sphacrophysine	113
Isoprine	113
Nanophyn	114
<i>F Adrenalin and adrenomimetic agents</i>	114
Adrenalin	114
Antiasthmocrin	116
Noradrenalin	116
Mesalon	117
Ephedrine	118
Isadrin	119
Naphthyzin	120
<i>F Adrenolytic agents</i>	121
Apressine	122
II Substances acting preeminently in the region of the endings of the motor nerves (curarelike drugs)	123
a) Drugs with a concurrent type of action	126
Diplocine	126
Paramyon	127
Dulsemine	128
Elatine	128
Mellicine	129
Condelphine	129
b) Drugs with a depolarizing type of action	130
Ditilin	130

Chapter III

ANTI-HISTAMINE DRUGS

Histamine	132
Dimedrol	133
Promethazine	135
Fenethazine	136
Diazolin	137

Chapter IV

CARDIOVASCULAR AGENTS

I Heart glycosides	138
<i>A Foxglove preparations</i>	141
a) Purple Foxglove preparations	141
Foxglove (purple and yellow)	141
Digloxin	143
Glloxin	144
Gitalen	144
Cordigit	145
Digipuren	145
Digilaside	145

b) Woolly Foxglove preparations	145
Lantoside	146
Dilaniside	147
Celanide	147
Abicin	148
c) Rusty Foxglove preparations	148
Digalen neo	148
Satituran	149
d) Ciliated Foxglove preparations	149
Digiclen	149
Digicil	149
<i>B Adonis preparations</i>	150
Spring Adonis or False Hellebore	150
Adonisid	150
<i>C Strophanthus preparations</i>	151
Strophanthin	151
Strophanthus tincture	153
<i>D Lily of the Valley preparations</i>	153
Lily of the Valley tincture	153
Dry Lily of the Valley extract	153
Convallatoxin	153
Convasid	154
Corglycon	155
<i>E Erysimum preparations</i>	155
Erysimin	156
Coresid	156
Cardiovalen	157
<i>F Canadian Hemp preparations</i>	157
Cymarín	157
<i>G Jute preparations</i>	158
Olitoriside	158
<i>H Silk vine preparations</i>	159
Periplocin	159
<i>I Oleander preparations</i>	159
Neriolin	160
<i>J Hellebore preparations</i>	160
Corelborin	161
II Agents lowering the excitability of the myocardium	161
Procainamide	161
Haws	162
III Agents which relax the smooth muscles of the blood vessels, of the bronchi and the organs of the abdominal cavity (spasmodic agents)	163
<i>A Nitrites and nitrates</i>	163
Amyl nitrite	164
	531

Sodium nitrite	161
Nitroglycerol	165
Aminotartrate phosphate	165
<i>B Isoquinoline derivatives</i>	166
Papaverine hydrochloride	166
Salsoline hydrochloride	165
Salsolidine hydrochloride	168
<i>C Purine derivatives</i>	169
Theobromine	169
Theobromine sodium salicylate	169
Theophylline	170
Aminophylline	171
Diprophylline	172
<i>D Esters of carbonic acids</i>	173
Aprophen	173
Tiphen	173
Diprophén	174
Gangleron	175
<i>E Various synthetic compounds and drugs of the natural origin</i>	176
Dibazol	176
Triacanthine hydrochloride	176
Khellin	176
Daucarin	177
Eucommia bark	178
Baikal Skullcap rhizome	178
Cimicifuga tincture	178
Southern Magnolia	178
Omelen	178
Downy flowered Astragalus	178
Bog Gnaphalium	178
Lime flowers	179
Angiotrophin	179

Chapter V

DIURETICS

<i>I Mercury diuretics</i>	180
Mercusal	180
Promeran	182
<i>II Carbonic anhydrase inhibitors</i>	182
Acetazolamide	183
<i>III Pyrimidine derivatives</i>	185
Aflacil	185
<i>IV Chlorothiazide and its analogues</i>	186
Chlorothiazide	186
<i>V Acid forming diuretics</i>	188
Ammonium chloride	188

VI Plant extracts and infusions used as diuretics	188
Juniper fruit	188
Bearberry leaf	189
Horsetail herb	189
Birch buds	189
Birch leaf	189
Cornflower flowers	189
Burdock root	189

Chapter VI

AGENTS WHICH STIMULATE THE UTERINE MUSCLES

I Ergot and the ergot alkaloids	190
Ergot Spurred rye	190
Ergotal	192
Ergometrine maleate	192
Ergotamine tartrate	193
II Various uterine agents	193
Cotarnine chloride	193
Pregnantol	194
Isoverine	194
European Barberry	195
Amur Barberry	195
Shepherd's Purse herb	195
Belony	195

Chapter VII

AGENTS ACTING PREEMINENTLY IN THE REGION OF THE SENSORY NERVE ENDINGS

I Local anesthetics	196
Ethyl aminobenzoate	196
Procaine hydrochloride	197
Dicain	200
Trimecain	201
Xycain	202
Sovcain	203
II Emollients and adsorbents	203
White clay	203
Talc	204
Magnesium trisilicate	204
Activated charcoal	204
III Astringents	205
<i>A Astringents of vegetable origin</i>	205
Tannin	205
Albumin tannate	205

Rutin	210
Vitamin D	211
Vitamin E	212
Sea Buckthorn oil	213
Vitamin K	241
Linol	245
II Agents stimulating leukopoiesis	246
Sodium nucleinate	216
Pentoxyl	246
Thesan	217
Leucogen	217
III Agents influencing the coagulation of the blood	248
<i>A Agents inhibiting coagulation</i>	248
Heparin	218
Neodicoumarin	250
Phenylin	251
Sodium citrate	251
<i>B Agents accelerating coagulation of the blood</i>	252
Lagochilus	252
Nettle leaf	252
Yarrow herb	252
Water Pepper herb	252
Hydropiperin	253
Cranberrybush bark	253
Arnica flowers	253
IV Hormone preparations	253
<i>A Pituitary preparations</i>	253
Adrenocorticotrophic hormone	253
ACTH zinc phosphate	256
Prolactin	256
Intermedin	256
Pituitary extract	257
Adiurecrin	257
Mammophysin	258
<i>B Thyroid gland preparations</i>	258
Thyreoidin	258
<i>C Parathyroid gland preparations</i>	259
Parathyroidin	259
<i>D Pancreas preparations and their synthetic analogues</i>	259
Insulin	259
Zinc insulin suspension	260
Protamine zinc insulin	260
Butamid	261
Lipocain	262
<i>E Preparations of female sex hormones and their synthetic analogues</i>	263
a) Estrogenic preparations of steroid structure	263
Folliculin estrone	263

Estradiol monobenzoate	264
Estradiol dipropionate	265
b) Estrogenic preparations of nonsteroid structure	266
Hexestrol	266
Diethylstilbestrol	267
Dimestrol	269
Octestrol	270
Sygethm	270
c) Hormones of the corpus Luteum (gestagens) and their analogues	271
Progesterone	271
Pregnin	272
F Preparations of the male sex hormones (androgens) and their synthetic analogues	273
Testosterone propionate	273
Testosterone enanthate	275
Methyltestosterone	275
Methylandrostendiol	277
G Gonadotropic hormones	278
Chorionic gonadotropin	278
V Drugs inhibiting the function of the thyroid gland	279
Methylthiouracil	279
Mercaptil	280
Potassium perchlorate	280
Diodotyrosine	281
Betasin	282
VI Enzyme preparations	282
Pancreatin	282
Pepsin	282
Acidin pepsin	283
Gastric juice natural	283
Gastric juice artificial	283
Lydasa	283
Ronidasa	284
VII Amino acids and protein hydrolysates	285
A Amino acids	285
Glutamic acid	285
Histidine	287
Leucine	287
B Protein hydrolysates containing a mixture of amino acids	288
Hydrolysin	288
TsOLIPK protein hydrolysate	288
Amino-peptid	289
VIII Plasma substitutes	289
A Heterogenous protein blood substitutes	289
Therapeutic serum (LSB)	289
Serum BK 8	290
B Synthetic plasma substitutes	291
Polyglucin	291
Polyvinylpyrrolidone	292

<i>C Saline and colloidal saline solutions</i>	293
Sodium chloride	293
Ringer — Locke solution	294
IX Sugars	294
Glucose	294
X Alkalis	295
Magnesium oxide	295
Magnesium carbonate basic	295
Calcium carbonate precipitated	295
XI Drugs which promote the excretion of salts	296
Cinchophen	296
Urodan	296
Urozin	296
Hypersol	297
XII Calcium and potassium salts	297
Calcium chloride crystalline	297
Calcium gluconate	298
Calcium lactate	299
XIII Phosphorus-containing drugs	299
Adenosine triphosphate	299
Muscle adenylic preparation (MAP)	300
Phytin	300
Phytoferrolactol	301
Calcium glycerophosphate	301
Lecithin	301
Lipocerebrin	301
Phosphren	301
XIV Drugs containing arsenic	302
Sodium arsenate	302
Duplex	302
Potassium arsenite solution	302
Arsenic acid anhydride	303
Arsenical tablets	303
Blaud's arsenic tablets	303
XV Drugs containing iodine	303
Potassium iodide	303
Sodium iodide	304
Calcium iodobenenate	304
Iod hypersol	304
XVI Drugs containing iron	305
Iron reduced	305
Ferrohematogen	305
Iron lactate	306
Hemochlorin	306
Ferrous carbonate with sugar	306
Ferrous sulphate	306
XVII Drugs containing cobalt	307
Coamid	307
XVIII Miscellaneous preparations obtained from animal blood and tissues	307

Luronit	307
Hyaloid body	307
Plasmol	308
Splenin	308
Hematogen	308
Hematogen children s	308
Endoxycin	308
XIX Biogenic stimulators	309
Aloe extract	309
Fibs	309
Pelodistillate	309
Peloidin	309
XX Antidotes and chelate forming compounds	310
Unitiol	310
Sodium thiosulphate	311
Ethylenediaminetetraacetic acid disodium salt	312
XXI Special agents for the prevention and cure of radiation sickness syndrome	313
Mercamin hydrochloride	313
Mercamin salicylate	314
XXII Special agents for treating alcoholism	314
Teturam	314

Chapter IX

ANTIMICROBIC AND ANTIPARASITIC AGENTS

I Chemotherapeutic agents	317
A Antibiotics	317
Albomycin	317
Levomycetin	318
Eulevomycetin	320
Synthomycin	321
Eusynthomycin	322
Streptomycin sulphate	322
Streptomycin calcium chloride complex	325
Dihydrostreptomycin	326
Dihydrostreptomycin PAS	327
Penicillin Benzylpenicillin	327
Benzylpenicillin procaine	331
Ecmovocillin	331
Bicillin	331
Phenoxymethylpenicillin	332
Erythromycin	333
Biomycin hydrochloride Chlorotetracyclin hydrochloride	333
Hydroxytetracyclin	336
Tetracyclin	337
Colimycin	338
Mycerin	339
Ecmolin	339
Nystatin	339
	539

<i>B Sulfanilamide drugs</i>	310
Sulfanilamide	311
Sulfanilamide soluble	342
Norsulfazol	313
Norsulfazol soluble	311
Sulfazine	344
Methylsulfazine	315
Sulfodimezine Sulfad mezine	315
Sulfacyl	346
Sulfacyl soluble Sulfacyl sodium	317
Urosulfan	318
Ethazole	348
Ethazole soluble	349
Phthalazol	349
Sulgin	3 0
Disulformin	351
<i>C Antituberculosis drugs</i>	352
a) Isonicotinic acid hydrazide and its derivatives	352
Isoniazid	352
Phthivazid	353
Saluzid	355
Saluzid soluble	355
Metazid	356
Larusin	357
b) Derivatives of para amino salicylic acid	357
Sodium para aminosalicylate, PAS	357
Bepase	358
c) Thiosemicarbazones	359
Tibon	359
d) Derivatives of thiocarbanilide	360
Ethoxyd	360
e) Miscellaneous compounds	360
Sulfonin	360
Juglone	361
Calcium aurothiopropanol sulfonate	362
<i>D Drugs for the treatment of protozoan infections</i>	362
a) Antimalarial drugs	362
Chlorguanide hydrochloride	362
Pyrimethamine	364
Methoxy diethylaminopropylamino quinoline	365
Chinocid	366
Cyclochin	367
b) Drugs for the treatment of leishmaniasis amoebiasis trichomoniasis and other protozoan infections	368
Solusurmin	368
Carbarsone	369
Emetine	370
Chiniofon	371
Trichomonacid	372
Aminochinol	373
Sanazin	374
<i>E Antisymphilitic drugs</i>	375

a) Organic arsenicals	375
Novarsenol	375
Myarsenol	377
Acetarson	378
b) Bismuth preparations	380
Biochinol	380
Bismoverol	380
Bithurol	381
Pentabismol	381
c) Mercury preparations	382
Mercuric ointment grey	382
Mercuric salicylate	382
Mercuric cyanide	382
Mercuric biniodide	383
F Anthelmintics	383
a) Drugs chiefly used for the treatment of intestinal hemotodiasis (ascaridiasis, ankylostomiasis, trichocephaliasis, strongyloidiasis etc)	383
Santonin	383
Santonica Levant wormseed	384
Piperazine	385
DiIrazine	387
Chenopodium oil	387
Gentian violet	389
b) Drugs chiefly used for the treatment of intestinal cestodiasis (teniasis, hymenolepiasis, diphyllorhynchiasis)	389
Male fern ethereal extract	389
Filixan	391
Aminoacetic acid	391
Pomegranate bark	392
c) Drugs chiefly used for the treatment of extraintestinal helminthiasis	392
Hexachloroethane	392
Sodium antimonyl tartrate	393
G Miscellaneous chemotherapeutic drugs	393
a) Nitrofurans	393
Nitrofurazone	394
Nitrofurantoin	395
d) Sulfones	395
Solusulfone	395
Sulfodiamine	396
c) Thiosemicarbazones	397
Cutizone	397
II Antiseptics	397
A Antibiotics for external use	397
Gramicidin S	397
Polymyxin M	398
Microcid	398
Sodium usnate	399
Imanin	399
B Haloid group	400
Halazone	400

Alkaline sodium hypochlorite	401
Iodoform	401
<i>C Oxidizing agents</i>	401
Hydroperit	401
Potassium permanganate	401
<i>D Acids and alkalis</i>	402
Salicylic acid	402
Benzoic acid	402
Bicarmint	402
<i>E Salts of heavy metals</i>	402
<i>a) Mercury preparations</i>	402
Mercuric chloride	402
Mercuric oxycyanide	403
Mercuric chloride ammoniated	403
Mercuric oxide yellow	403
Diocid	403
<i>b) Silver preparations</i>	404
Silver protein	404
Colloidal silver	404
Bactericidal paper	405
<i>c) Lead preparations</i>	405
Lead plaster simple	405
<i>d) Zinc preparations</i>	405
Zinc sulfate	405
<i>F Formaldehyde group</i>	406
Lysoform	406
Methenamine	406
Calcex tablets	406
<i>G Phenol group</i>	407
Resorcinol	407
Ichthammol	407
Albichthol	407
Salol	408
Benzonaphthol	408
<i>H Petroleum products Mineral oils Balsams</i>	408
Naftalan petroleum refined	408
Vinilin	409
Cygerol	409
Polymerol	410
Aviol ointment	410
BF 6 cement	410
<i>I Dyes</i>	410
Acridlavine	410
Triazol tablets	411
Ethacridine	411
Methylene blue	412
Brilliant green	413
Novikov's antiseptic liquid	413
<i>J Hydroxyquinoline derivatives</i>	413
Hydroxyquinoline	413
Contraceptin	414
<i>K Preparations used in the treatment of fungous skin diseases</i>	414
Undecin	414
Zincundan	414

Dustundan	414
Thallium plaster	414
Epilin plaster	415
Onycholysin	417
<i>L. Phytoncide preparations</i>	418
Garlic tincture	418
Alhlsat	418
Alhlcep	418
Alliglycer	418
Ursall	418

Chapter X

DRUGS USED FOR THE TREATMENT OF NEOPLASMS

I Chemotherapeutic drugs	419
<i>A Derivatives of bis (2 chloroethyl) amine</i>	419
Novembichin	419
Dopan	421
Sarcosine	422
Embitol	424
<i>B Compounds containing ethylene imino groups</i>	425
Thiophosphamid	425
<i>C Esters of disulfonic acids</i>	426
Myelosan	426
<i>D Derivatives of colchicine</i>	427
Colchamine	427
<i>E Antimetabolites</i>	428
Mercaptopurine	428
II Symptomatic preparations for patients with malignant neoplasms	429
Birch fungus extract	429
Neocid	429

Chapter XI

DIAGNOSTIC AGENTS

I Roentgenopaque media	430
Sergosin	430
Cardiotrast	431
Triotrast	432
Iodolipol	433
Iodoalphyonic acid	434
Bilignost	434
Iodognost	435
Barium sulfate	436
II Other diagnostic agents	436
Indigo carmine	436
Bibliography	438
Alphabetical index	516

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